THE USE OF INPUT/OUTPUT DESCRIPTIONS FOR HIGH COST HEALTH COMPONENTS: KIDNEY-RELATED HEALTH SERVICES

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CHAPTER ONE

I. INTRODUCTION

Kidney disease is an agglomeration of infections and states of hypertension in which the kidneys fail to perform the vital process of removing fluids and waste compounds from the blood. Kidney disease can attack persons of any age, but it is particularly common in the years between 30 and 50, years of highest productivity of the average worker. Thus, kidney disease is both a health problem and an economic problem.

An estimated 58,000 Americans of both sexes and of all ages die each year of irreversible kidney failure.[1] The most common urinary tract disease is a mild infection present in an estimated 3,300,000 individuals at a given time. Advanced cases may spread to the vital organs, and, if undiagnosed and untreated, may eventually lead to serious kidney impairment and eventual fatal uremia. It is with this serious end-stage of the disease continuum that this study is concerned.

Technological breakthroughsin the past ten years have made technically feasible the widespread delivery of remarkable new forms of health care to combat the end-stage of renal failure. The first treatment modaility is dialysis, which cleanses the blood of impurities and helps restore chemical balance. One type of dialysis, peritoneal dialysis, uses the lining of the patient's abdomen as a filter to remove waste products from the body. The second type of dialysis, hemodialysis, employs an artificial kidney machine for the same purpose. Either type of dialysis may be used for the patient with

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[1] U.S. Department of Health, Education and Welfare, Public Health Service, Activities of the Kidney Disease Control Program, George E. Goodman (Feb. 15, 1968).

acute kidney failure--where the inability of the kidney to function is sudden and may be temporary. The second is of particular importance in treating chronic kidney failure, the result of long-term, progressive kidney destruction.

The other new development is kidney transplantation which makes it possible for a surgeon to implant a kidney from a donor (live or dead) into the patient. Given compatible organs, the new kidney will function for the patient as his natural organ did.

Although much research remains to be done to perfect these technologies, the problem of the economics of the health care delivery system looms larger than the technical question of workability. As Hinman wrote in 1972:

> Nowhere in the health care industry does the same gap exist between technology and delivery as in the area of treatment of patients with end-stage renal disease. Technological developments in the past ten years have made possible the rapid expansion of programs to provide patients with chronic dialysis therapy . . . techniques of organ harvesting, preservation, and transplantation have made renal homotransplantation a service entity and no longer a research tool. However, the funding mechanisms to develop the resources have lagged far behind. A conservative estimate is that annually 7,000 ideal candidates for end-stage therapy will die of renal disease unless they receive either a successful transplant or chronic hemodialysis therapy.[2]

Thus, one confronts a situation where the costs of treatment are very high, the choice of technologies is available and the relative success or failure of the various treatment programs must be analyzed to achieve an adequate assessment of costs and benefits.

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[2]Edward J. Hinman, et al., "An Economic Model as a Health Decision Making Tool," paper presented at the Annual Meeting of the Southeastern Dialysis and Transplant Association, Biloxi, Mississippi, August 11, 1972.

As government expands its commitment to fund treatment of chronic diseases, planners and health administrators should find it increasingly necessary to have reasonable forecasts of future capacity utilization.

Federal action, in the form of an amendment to the Social Security Act, serves as a commitment to funding of treatment for chronic renal disease (kidney failure). The "Kidney Amendment" (Section 2991, PL 92-603, Social Security Amendments of 1972) was to be effective by July 1, 1973, making all end-stage renal patients eligible for Medicare regardless of age. The Department of Health, Education and Welfare could not meet the "vague" maximal standards in the required time, however, and issued interim guidelines for kidney treatment center certification and reimbursement. The long-range implementation of this law should cover "virtually all persons (with) end-stage renal disease." (REF 277)

A. The Forecasting Model

It is in this context that a forecasting model has been developed in the current study for the renal disease-treatment system. We hope that the result can serve as a prototype for efforts on other disease-treatment systems. The regional forecasting model has two components: a forecast of patient flows through the system, by treatment mode, and a derived estimate of projected unit costs, by treatment mode. The disease-treatment component will be estimated, from patient data, as a first-order Markov process, subject to entry through birth, and exit through death. Output of this model, combined with a treatment-specific cost vector, can be used to forecast costs and utilization rates.

The model focuses on regional forecasting because the law makes regional officials responsible for systems to treat renal disease. HEW's interpretation of PL 92-603 calls for certification, not only of individual treatment facilities but also for "networks," or regional treatment systems. Since Comprehensive Health Planning Agencies were given responsibility for designing networks, the need for developing a regional data base and applying it to planning system growth becomes obvious. The National Health Planning and Development and Health Facilities Assistance Act replaces expired Comprehensive Health Planning Programs with "a single new program of state and area-wide health planning and development..." Health planning agencies will be responsible for area planning and will have, annually, to "establish or revise a long-range goal plan (LGP) and a short-term priorities plan (SPP)." The same will be true for State Health Planning and Development Agencies. (REF 285)

In addition, there are strong *a priori* arguments for a regional focus that relates to parameter estimation. Treatment systems differ among regions, reflecting varying population densities, resource availability and preferred medical practice. These structural differences should help shape the stochastic processes governing patient flows.

B. Markov Methodology

This project develops a mechanism for forecasting utilization rates and costs of delivering medical care for individuals with chronic renal disorders. The techniques used here will, it is hoped,

prove of general applicability in dealing with planning for other high cost health services.

Models have been built to forecast for three areas: a regional "megalopolis," a large state, and a group of rural states. A breakdown of this kind will permit more accurate specification of cost and patients' movements in the system, and will indicate the loss in precision that more geographically-comprehensive models might suffer.

This model consistsof two parts:

1. Parameter estimation: specification of patient states or condition/treatment modes, the nature and timing of movement among these states and the implications of demographic changes for present and future utilization of systems which treat kidney failures.

2. Cost analysis: estimate of regional differences in charges for available treatment systems.

The resulting model uses principles derived from the input/output matrix methodology and transitional probability analysis to predict the final outcomes of a number of rounds of treatments, and associated total costs by regions.

The model characterizes the patient as existing in one of a finite number of states at a given point in time with an arbitrary probability distribution describing the length of stay in a state. Transitions between states are assumed to follow that of a stationary finite Markov chain. The model can then generate (1) the probability that an individual will be in a given state at time "t", given that he is in a previous state at time "t-1", (2) the probability distribution on reaching various absorbing states (death) and (3) the probability distribution associated with the time elapsed on passage from state-to-state.

C. Regional Characteristics

Three regions have been chosen for analysis, using two selection criteria: demographic mix and data availability. These include a "megalopolitan" area (Boston-Worcester-Providence), a group of rural Southern states, (Mississippi, North Carolina, South Carolina, Tennessee and Virginia), and one large demographically-diverse state, California. Further discussion of regional factors will appear later in an analysis of parameter estimates.

Table 1-1 shows that the South and California have populations that are slightly younger relative to the population of the Boston megalopolis. Of particular note is the fact that 13% of the Boston population is over 65 years, whereas the proportion for other two regions is 9% each.

In Table 1-2 comparison is made of kidney disease-treatment systems among the regions, using data gathered from various state and federal sources. The project could secure only limited Southern data from official sources. Comprehensive statistics for North Carolina were unavailable, and the information on Mississippi and Tennessee come from a report on facilities in the Memphis-Jackson area. Data specific to the Boston megalopolitan area were unavailable, but since most of the Massachusetts dialysis and transplant activity occurs within the Boston SMSA, Table 1-1 and 1-2 show figures from Massachusetts state reports. Data from California proved most current and complete.

Column 1 of Table 1-1 suggests that the South relies relatively more heavily than other regions on home dialysis for

patients. It is interesting to note, however, that in the urban Memphis - Jackson area, reliance on home dialysis (29%) more nearly resembles the fraction for the Boston megalopolis (30%). Virginia (39%) and South Carolina (43%) stand out as highly dependent on decentralized treatment. California (14.8%), a state with mixed rural and urban characteristics, depends least on home dialysis.

The limited information available on home dialysis training suggests that marginal changes in the distribution of patients among treatments will not change greatly (see column 3). Eight out of 100 institutional dialysis patients train for home dialysis in the Memphis - Jackson area, compared to 36 of 100 in Virginia.

Column 4 suggests that, on average, 27 of 100 chronic dialysis patients in Massachusetts are transplanted (based on the year of observation). We suspect that the true base for this figure should include chronic patients who traveled to Boston from other states (and foreign countries) to take advantage of that area's medical expertise. More recent figures would probably reveal less discrepancy between Boston and California (12 per 100), Virginia (5 per 100) and Memphis - Jackson and South Carolina (1 per 100).

Prevalence and incidence figures have not been collected for regions, and the estimates in columns 5 and 6 should be viewed with considerable reservation. There appear to be more chronic patients /100,000 population in California, than in the other regions. Massachusetts 1.73/100,000 seems surprisingly low, in view of the concentration of medical facilities in the Boston area.

Patients/chronic dialysis machine (column 2) suggests the rate of capacity utilization is higher in urban centers, like Memphis - Jackson (2.02 patients/machine) and urbanized states. (California, 2.68 patients/machine). Virginia and South Carolina show lower utilization rates (1.59/machine and 1.00/machine respectively).

Finally, mortality rates for kidney disease, defined here conservatively to include ICDA codes 580-584, hypersensitivity disease, are higher on average in the South than in California or Massachusetts South Carolina, the most "rural" of the Southern states on this list, has the highest death rate, 5.0/100,000, and California the lowest, 3.0/100,000 in 1968.

Table 1-1
Demographic Characteristics of the Regions
Age-Sex Distribution, January 1972 and January 1973

(By Thousands)

	January 1972				January 1973			
	M	F	Totals	Age Group Total	M	F	Totals	Age Group Total
Boston Megalopolis Age Group								
0-14	488.7	477.7	966.4	.236	476.2	465.2	941.4	.226
15-44	851.8	915.5	1,767.3	.431	871.3	936.5	1,807.8	.434
45-64	377.8	466.8	844.6	.206	379.3	468.3	847.6	.204
65 +	191.5	328.7	520.2	.127	208.5	358.2	566.7	.136
	1,909.8	2,188.7	4,098.5	1.000	1,935.3	2,228.2	4,163.5	1.000
Southern Rural Age Group								
0-14	2,535.5	2,436.3	4,971.8	.263	2,558.5	2,458.8	5,017.3	.261
15-44	4,040.0	4,555.0	8,595.0	.454	4,130.0	4,657.0	8,787.0	.456
45-64	1,737.7	1,960.0	3,697.9	.195	1,761.2	1,986.7	3,747.9	.195
65 +	695.3	960.8	1,656.1	.088	713.8	986.3	1,700.1	.088
	9,008.5	9,912.3	18,920.8	1.000	9,163.5	10,088.8	19,252.3	1.000
California Age Group								
0-14	2,574.0	2,473.0	5,047.0	.248	2,518.0	2,419.0	4,937.0	.241
15-44	4,652.3	4,652.3	9,304.6	.457	4,744.8	4,744.8	9,489.6	.463
45-64	1,988.9	2,154.3	4,143.2	.203	2,009.4	2,176.8	4,186.2	.204
65 +	767.0	1,103.5	1,870.5	.092	783.0	1,112.7	1,895.7	.092
	9,982.2	10,383.1	20,365.3	1.000	10,055.2	10,453.3	20,508.5	1.000

Source: Estimated from U.S. Bureau of the Census Current Population Report P-25 Number 500, 518, Estimate of the Population of States by Age

Table 1-2

Selected Characteristics of Renal Disease Treatment Systems, by Region

	% Dialysis Patients On Home Dialysis	Patients/Dialysis Machine (Chronic)	Patients training for Home Dialysis / Total Institutional Dialysis Patients
	(1)	(2)	(3)
Region I			
Massachusetts	30%	N/A	N/A
Region 2			
Memphis - Jackson	29%	2.02	.084
South Carolina	43%	1.00	N/A
Virginia	39%	1.59	.357
Region 3			
California	15%	2.68	N/A

Sources: Region 1:

Phillips, Harry T. et al, Massachusetts Kidney Disease Planning Project: The Final Report (1970)

Medical Care and Education Foundation, Inc. Tri-State Regional Medical Program, New England Regional Kidney Program (1970)

Region 2

Pierce, James C., The Renal Program in Virginia Virginia Regional Medical Program: Kidney Committee (1970)

South Carolina Department of Health and Environmental Control State Renal Program (1974)

(continued....)

Table 1-2 (Continued)

Selected Characteristics of Renal Disease Treatment Systems, by Region

	Transplants Total Chronic	Chronic Patients Total Population (00,000)	Incidence (00,000	Mortality: Nephritis Nephrosis (00,000) (1968) ICDA Codes 580-584
	(4)	(5)	(6)	(7)
Region I				
Massachusetts	.276	1.73	N/A	4.7
Region 2				
Memphis - Jackson	.014	7.39	4.89	4.9
South Carolina	.008	3.69	N/A	5.0
Virginia	.053	2.83	N/A	4.9
Region 3				
California	.120	11.3	4.48	3.0

Sources, Continued:

Med-South Medical Center Council for Comprehensive Health Planning, Inc.
End-Stage Renal Disease Plan (1974)

Region 3:

California Kidney Disease Information System (Statistical Summaries)

"Chronic Hemodialysis Patients: Age by Year at First Dialysis" (1974)

"Hemodialysis Facilities, Patients, Beds by County" 1974

"Transplant Statistics - 1972, 1973, 1974"

All Regions:

U.S. Department of HEW, Regional Medical Program Services, Kidney Disease Services, Facilities and Programs in U.S. (1971)

CHAPTER TWO

II. METHODOLOGY

This study uses statistically estimated Markov transition probabilities to describe and forecast the movement of patients among various kidney disease-treatment "states". The discussion that follows covers the nature of these states, a theoretical treatment of the basic Markov assumptions, and a critique of the data sources used in the estimation process.

A. Definition of Patient States

In this study, we shall identify "states" in which groups of patients might be found at a given time. We locate a patient in one state only for a particular time period (day or month, see below). Analysis and forecasting about this disease-treatment system will involve transition rates of patients from one state to another.

The process of defining and refining state definitions reveals the implicit cost, in loss of specificity, of gaining computational flexibility and using existing data sources. We began with a list of 113 states, which spelled out severity and nature of kidney disease, type and location of treatment. However, because of data limitations the model was tested using only seven states.

In the current presentation of the model, the following states were used. The numbering and inclusion of states in specific applications differs according to the data source, as will be made clear later.

States	Definition
Well	Applies to persons not in the chronic kidney disease-treatment system.
Stable	Applies to persons with a functioning kidney transplant.
Dialysis	Applies to persons now receiving dialysis (cleansing of blood and maintaining body's chemical balance by filtration through semi-permeable membrane).
Institutional hemodialysis	Dialysis by means of artificial kidney device, in hospital or limited care facility, under supervision.
Peritoneal dialysis	Dialysis treatment which uses patient's peritoneum for filtration process: here assumed done in institution, under close supervision.
Home dialysis	Hemodialysis performed in patient's home by patient, under minimal supervision.
Transplant	Kidney graft
Live donor transplant	Kidney donor of any relation to recipient
Cadaver donor transplant	Kidney donor deceased
Death	

The model relates only to the chronic kidney disease-treatment system; there are no data on reversible acute kidney disease patients. The choice of the states in the parameter estimation to follow was completely data-determined. The RLA research team had hoped that data would yield an opportunity to make the following distinctions and inclusions:

1. Acute Versus Chronic Patients

A patient may suffer temporary loss of kidney function, but under treatment, the condition proves to be reversible. Within a span of less than three months he has regained the natural renal functions. This situation is the characterization of acute kidney disease. By contrast, the chronic kidney patient has forever lost the use of his kidney, and must be maintained through dialysis or transplant or face death.

Unfortunately, none of the data showing patient states adequately assesses the incidence of acute kidney disease. The National Dialysis Registry appears to ask for this information, but instructions were sent to respondents asking them not to include acute cases in the reports. It appears, however, that some cases of reversible conditions nonetheless were reported. In any case, there are insifficient data to obtain an understanding of transitions to and from acute states.

In order to obatin an estimate of the occurrence of acute conditions, RLA engaged in primary data collection in seven hospitals in Washington, D.C. Data on disease occurrence is given in Table 2-1.

None of the selected hospitals indicated serving a particular "catchment area"; rather, each specifically stated that services were provided to its immediate community and the Washington community at large. Therefore, an incidence estimate was not permitted from available data.

2. Disease-Specific Information

The medical advisory committee for the project urged the separate

consideration of disease types within the kidney disease classification: glomerulonephritis; pyelonephritis; hereditary kidney disorder; and vascular and other kidney disorders. By far the most common diseases are the first two, and it was the judgment of the medical advisory committee that the transition probabilities would not differ significantly between pyelonephritis and glomerulonephritis. Furthermore, it was noted by the National Dialysis Registry that the classification of kidney disease type was quite unreliable in their coding system. It was therefore decided, in the interest of accuracy and economy, to ignore disease-specific information in the construction of the matrices.

3. "Waiting for Transplant" or "Tissue Typed"

This state was originally suggested in the Scope of Work. However, the category is not mutually exclusive, overlapping with various forms of dialysis, and thus is ineligible in a Markovian formulation which demands exclusivity of categories. Furthermore, only the ACS/NIH Transplant Registry could furnish data on dates of tissue-typing; and this data source is biased in that only persons who have experienced transplants are included. Since conditions of eligibility for receiving a transplant are severe, the sample is clearly biased and unusable in a full national model.

4. Training for Home Dialysis

This state is an important phase in any cost analysis, but it is also repetitive with institutional dialysis, and therefore cannot be considered as a separate category in the model.

5. Distinctions Among First, Second and Third Transplants

These distinctions were at one time considered useful in the project. However, it was found that the sample size was too small to make useful distinctions.

6. Distinctions Between Cadaveric and Live Transplant Donors

It is agreed by most medical specialists that this distinction is important in determining probability of successful transplant. However, data from the National Dialysis Registry, the primary source of transitions information, did not distinguish between sources of donor kidneys. Hence data constraints forced the dropping of this useful category.

7. Location of Institutional Dialysis

This information can be broken down into useful categories: hospital in-patient; hospital out-patient; walk-in center; mobile unit, etc. Hospital types are also distinguished by Nakamura and Parker[5] into teaching and non-teaching institutions.

8. Migration States

The full discussion of the forecast model includes reference to regional and out-migration as an absorbing state. Data on treatment sites were inadequate to derive empirical estimates

5 Masao Nakamura and Roger Parker, A Stochastic Control Approach to the Evaluation and Design of Health Services Systems with an Application to a Kidney Disease Control Problem. (REF 335)

however, and the state was omitted in the matrix operations.

B. Markov Theory

The rules we applied to the analysis of patient data are based on the assumption that this system behaves like a Markov process. A Markov process, in which units (patients) move from state to state over time, is defined by conditional probability distribution which relate the states of the system at time (t) with the states at (t-1).

We further assumed a first order, homogeneous process. A first order process links contiguous states and makes the state at time (t) depend only on the state at time (t-1). Information from t-2....t-n has no bearing on the one-step transition. Thus, if we examine the probability that a patient on dialysis will, next month, receive a transplant, the process can be described:

$$P\ (\text{Transplant } (t)/\text{Dialysis } (t-1)) = p^{(t)}_{\substack{\text{Dialysis}\\ \text{-Transplant}}}$$

or, more generally,

$$P\ [X(t)=j/X(t-1)\ =i] = p_{ij}(t)$$

In a non-homogeneous system, the P_{ij}'s can vary depending on t. In a homogeneous system, however, the one-step transition probability remains constant, that is:

$$P_{ij}(1) = P_{ij}(2) = \ldots = P_{ij}(n) = p_{ij}$$

In the homogeneous case, one can talk about a Markov matrix which gives the constant one-step probabilities of transitions in

one time period. If one knows the initial states of the system, one can show where system members will be one period away by multiplying,

$$n(t-1) \times P = n(t),$$

where n's are vectors with numbers of system members distributed across states, and P is the Markov matrix. Longer period forecasts can be done by using powers of the P matrix, that is:

$$n(o) \times P^t = n(t)$$

Use of the Markov framework may be invalid if, by ignoring the influence of patient states prior to (t-1), valuable historical information that might improve the model's prediction performance, is suppressed. A first-order chain discards data from (t-2, t-3...), and logs changes in individual states by passage of calendar time. Weiss and Zelen,[1] in a study of acute leukemia, have argued that disease transition probabilities have to relate to progress of the disease itself, rather than passage of weeks or months. The probability of a move out of a state will, in this light, vary with the elapsed time in that state (and/or the frequency and duration of stays in other prior states). There are three ways the problem might be approached:

1. Impose a semi-Markov process on the data. In this approach, holding times in states, or time intervals between "successes" defined as moves, are considered random variables with distributions (usually geometric or Poisson) of their own. Weiss and Zelan chose this approach in their own study. Goyal has discussed the statistical problems of estimating parameters in a semi-Markov process.[2]

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[1]REF 245.
[2]REF 18.

2. Construct a cumulative inertia model, in which each fundamental state is classified by duration of stay. Dialysis, for example, might be divided into three new states, identified as "on dialysis, 1) 1-3 months, 2) 4-6 months, 3) 7+ months." The transition options then include moving to another fundamental state or staying and progressing within the state to a higher time classification. (This technique is discussed in Bartholomew).[1] A variant of this approach involves building prior states into the fundamental states. For example, rather than a single transplant state, subdivide by the number of the transplant.
3. Estimate an rth-order Markov process, r 1, in which the underlying conditional probability statement is:

$$P\ \{X(t) = j/\ X(t-1) = i,\ X(t-2) = k, \ldots, X(t-r) = m\} = P(t)_{m\ldots,k,i,j} \qquad 1 \leqslant r$$

These approaches add mathematical and computational complexity beyond the scope of this report.

C. Review of Data Sources

We shall use two main sources of data to estimate transition probabilities:

The Research Triangle Institute National Dialysis Registry (RTI)

The American College of Surgeons/National Institute of Health Organ Transplant Registry (ACS)

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[1] REF 5.

The Medicare Records of the Social Security Administration have been used to provide cost estimates.

All three of these sources overlap in coverage over a broad area, and all cover, in greater or lesser detail, the experience of end-stage patients. They appear to define their terms identically. Discrepancies occur, in areas of overlap, when two sources differ in the amount of detail provided; on transplants, for example, the ACS and SSA forms add information on tissue typing that the RTI forms lack. "Cause of death' may also be interpreted differently, but we expect that the variation in this response is probably as wide <u>within</u> a source (reflecting views of diverse physicians) as it is <u>among</u> sources.

1. <u>National Dialysis Registry</u>

The Research Triangle Institute, in the latter years of the 1960's, contracted with the Public Health Service (Kidney Disease Control Program), the National Institute of Arthritis and Metabolic Diseases and the Veterans Administration to collect medical and sociological data on all chronic dialysis patients in the nation. First data-collecting efforts, following an ambitious but disappointing pilot project, took place in 1970. These data have been updated on a regular basis, and consist of patient records supplied by cooperating centers. Compliance is voluntary, though a small fee is paid to cover clerical costs. The records are entered into RTI's National Dialysis Registry computer files.

The RTI data are drawn from two series of forms: Series I, recorded prior to November, 1972, and Series II, recorded after this date. Comments of RTI staff suggest that Series II data are superior in coverage and accuracy to Series I data. Since Series I data are only available in hard copy, we have used only Series II data in the estimations. In the regions for this study, RTI files contained information on 3360 patients, of which 840 were chosen randomly for parameter estimation, a 25% sample.

RTI data are recorded for each patient on two forms; (1) A record file lists current status of patients in the system, with a fairly complete patient history. Transplants are recorded on this form, along with limited information about transplant failure. (2) Transactions files indicate major changes in type, location of treatment, movement among treatment centers, and loss of follow-up. For each patient in the system, then, there will be at least one updated record file, and one or more transactions files. Patients who have died since 1972 are included, whether or not they entered the system before or after 1972.

Certain gaps and problems of interpretation have arisen as we have attempted to use the RTI data. Ideally, as an information system, the combined record-transactions files should constitute a complete patient history. Unfortunately, in several cases, patients with coded changes in location of treatment or treatment type on the record file have no corresponding transactions file coverage of these changes. Mis-matching occurs in the other direction as well. Project staff discovered evidence of changes from transaction

file records that were not entered on the record file. In some cases, the number of location changes, for example, listed on the record file failed to correspond with the number of changes in the transactions files. It may be that gaps in one or the other files tend to be filled if investigators carefully examine both files for each patient. But since the gaps appear to be distributed in an unsystematic way, coding time is greatly increased. Moreover, the files cannot be used systematically to cross-check the validity of certain entries.

A major gap in the transactions file format, apparently related to RTI's concentration on dialysis, is failure to record a transplant as a transaction. This omission is peculiar, because the record file permits entry of several transplants for each patient. Provided the data on the record file are accurate, of course, this problem may not be serious, but the theory behind this approach is puzzling.

For the purposes of this project, the recording of transactions and patient personal history dates by month and year rather than by day, makes estimation of the Markov process less accurate. It would seem, moreover, that users with interest in purely biostatistical analysis would need the same daily reference points for their work, since a day constitutes the smallest usable time unit within which a single transition is possible. The value of daily data depends in part, of course, on the accuracy and dedication of respondents who complete the RTI forms; sloppy record-keeping and/or a failure to file transaction changes promptly can compromise the value of a system that aims to greater precision of coverage.

As might be expected, RTI coverage of transplant information is sparse, in comparison with detail recorded on dialysis. Added information which would be of use includes type of donor, and whether or not tissue typing was done. What appears to be a successful transplant, according to RTI files, may simply disguise loss of follow-up. Some explicit indication of the recipient's condition, up-dated on a regular basis, would be useful.

Though designed to cover dialysis of end-stage patients, there is some evidence that patients with acute failure have occasionally been included. Entries of patients on hemodialysis of one month, after which, according to RTI codes, "dialysis is no longer needed," is either acute failure (properly diagnosed) or (improperly diagnosed) end-stage failure. The data are too few to permit full analysis of system use by acute patients. This is a serious omission, since resources committed to chronic cases may find potential use in treating acute cases.

Coding system inaccuracies were discovered. Under RTI's classification scheme, most of the patients erroneously appeared to be on peritoneal dialysis, and a large fraction of these on <u>home</u> peritoneal dialysis. Later inquiry identified this as an error on the coding sheet used as a key.

Failure to record date of birth accounted for the largest single gap in patient records that we could discover. Dating other major transactions appeared to be fairly complete, though transplant dates were occasionally omitted.

2. Organ Transplant Registry

The American College ofSurgeons-National Institute of Health Organ Transplant Registry strives to maintain records on organ transplants of all kinds done in the United States and abroad. In 1969, the ACS group began collecting data on non-renal grafts and by 1971, renal transplant data collection was begun. ACS absorbed the function of the Kidney Transplant Registry, founded in Boston in 1963.

The ACS material is available on computer file, and predates both RTI and SSA data by several years. This project had access to all patient records on kidney transplants, but to permit comparisons with RTI data, direct analysis of ACS data was restricted to the period since 1972. Parameter estimation utilized the entire population of transplant patients from the three regions, 1101 cases.

Each patient's history is recorded on two types of cards: one gives all historical data and information surrounding the patient's transplant (one card for each transplant). The other card(s) follow the patient's post-transplant progress.

The history recorded by this system is, by design, partial in that pre-transplant medical facts, about dialysis type and location, are not included. The patient enters the system on first transplant, and medical history begins from this point. In general, the sequences described by the two sets of cards are consistent (little mis-matching of dates and the like), which make them plausible.

Given this format, however, the ACS data are as deficient in dialysis detail as the RTI are in transplant detail. Only post-transplant

dialysis experience is recorded. Moreover, it is impossible to determine type (hemodialysis or peritoneal dialysis) and location (home, institution) of treatment. Information on donor, tissue typing, drug and ancillary surgical activities surrounding the transplant is, of course, thorough (in contrast to RTI records).

ACS data are recorded on a daily basis, a fact which is of importance to users with statistical analysis in mind. Of course, it is true, as mentioned above, that requiring dating precision of this type may spawn a certain amount of guesswork among record keepers. However, because the filing is the responsibility of physicians directly involved, one may be somewhat more confident of these data than of the RTI data.

Follow-up coverage seems to be of uneven quality, with some transplant centers maintaining coverage up to the most recent dates available (early 1974), but some failing to follow patients with transplants done over two years ago. As with RTI data, the major data gap was in age information. Ten or twelve patients were recorded as being on dialysis several months after an earlier follow-up card pronounced them dead!

It is difficult to judge the quality of the data sources, since primary testing of quality was beyond the scope of this contract. However, it ispossible to comment on gaps in coverage, on comparative coverage and on some tests against the best independently gathered state data available (California Kidney Disease Information System).

A check of data collected by the California Kidney Disease Information System against RTI figures reveals serious undercounting by the Registry. Table 2-2 compares RTI figures for individuals who began long-term dialysis in 1972 and 1973 with CKDIS figures. The coverage fraction, $\frac{(RTI)}{(CKDIS)}$, drops dramatically from 1972 to 1973. One suspects the reporting lag for RTI forms (3-6 months) explains much of this result. One has no way of assessing the probable bias from the RTI undercount, however, since there is no information on which centers delay in reporting.

ACS data on transplants in California during 1972 and 1973 are also checked against CKDIS fugures. The results appear in the last column of Table 2-2. Column (5)/(4) shows that ACS covers about 65% of transplants for California, and that this ratio changes little for the two years covered by this study.

Columns 3 and 4 show a more serious problem of undercounting transplants in the RTI data. It is interesting to note here, however, that the discrepancy increases only slightly from 1972 to 1973.

It would seem, then, that forecasts for California based on RTI data would be suspect from the start because of an undercounting of unpredictable size and bias. RTI officials seem confident that, nationally, their data cover 90% of the chronic dialysis population.

It may be that records on patients who began dialysis prior to 1972 are considerably more complete than those examined by this project. This is small comfort for the forecaster, however, who hopes for usable data from recent periods that more accurately reflect the

most current medical techniques and patterns of flow within the system.

In addition to gaps in the data mentioned above, we failed to secure treatment-specific regional in and out-migration figures. Such data are, of course, quite important for regional modeling of this kind. One would expect considerable "exporting" of kidney treatment services (patient in-migration) by centers such as Boston and California, whereas rural regions probably import such services (patient out-migration).

D. Structure of the Model

A model to forecast patient flows, based on the fundamental Markov matrix, must take into account net changes in the demographic characteristics as well as disease-related changes in the patient population. What follows is a discussion of the broad features of the model. Readers interested in a more technical discussion should consult Appendix A.

The heart of the model is a Markov matrix with six transient states and one absorbing state (death)
(for the RTI estimates):

1. Well
2. Stable
3. Institutional hemodialysis
4. Peritoneal dialysis
5. Home hemodialysis
6. Transplant
7 Death

Separate matrixes were estimated for each of 4 age groups:

1. 0-14 years
2. 15-44 years
3. 45-64 years
4. 65 + years

Sets of age-specific matrixes were estimated, by sex, for each of the three regions:

1. Boston - Worcester - Providence (Boston megalopolis)
2. Southern States: North and South Carolina, Virginia, Tennessee, Mississippi
3. California

The population for each region is aged during the time period of the forecast by multiplying each element of the age specific matrix by an age coefficient. Thus α % of the population in each state ages from one age group to the next in a given time period, whereas $(1-\alpha)$ % remain in their initial age category. A larger regional disease-treatment matrix contains 4 "stayer" matrixes (allocating members of given age group that stay in the group) and 4 "mover" matrixes (moving a fraction of an age group to the next higher age category); a vector of death rates, for each of the six transient states and four age categories; four rows of zeroes reflecting the impossibility of returning from death to any one of the six transient states; and a vector of 1's showing the perfect recurrence probability of the absorbing state.

Death constitutes the principal outflow from this system. To make the model useful for forecasting, a birth coefficient is added to bring the individuals into state 1 of the youngest age group. Ideally, regional migration should be handled by separating out-migration

(which could be treated as an absorbing state) from in-migration, which could be added to the diagonal elements of the stayer matrixes. Data limitations required that a migration adjustment be made that takes account of net changes, however. This adjustment coefficient was added to the diagonal elements of the stayer matrixes. The final form of the forecast matrix, then, had the following structure:

b (a column of birth coefficients)

\+ m (diag) (an adjustment coefficient for net migration, added to diagonal elements of the stayer matrix)

\+ $P^{(a)}$ (an age-adjusting treatment matrix)

Under certain assumptions about the nature of the treatment matrixes and the behavior over time of input and output coefficients, it is possible to speak of the system tending toward a steady state distribution of the population. A general steady state solution to this system would show the population tending toward a stable fraction in each age and disease category; that is, one could think of X% of the population aged 0-14 being on dialysis in the long run. Of course, this X% would involve different individuals over time.

Table 2-1

Occurrence of Kidney Disease
Patients Diagnosed Acute or Chronic,
for the Period January, 1972 through December, 1974,
by Selected Hospitals in the Greater Washington, D.C. Area

	Year	Total Admissions	Acute	Chronic
	1971	13,254	6	71
I. Howard University Hospital	1972	12,264	1	75
	1973	11,916	6	85
	1974	12,137	15	105
II. George Washington University Hospital	1970	20,647	10	100
	1971	19,382	8	41
	1972	18,781	7	115
	1973	19,381	13	134
	1974	20,857	6	100
III. Washington Hospital Center	1972	35,098	19	147
	1973	34,689	16	111
	1974	35,392	16	98
IV. D.C. General Hospital 1/	1972	19,129	1	26
	1973	17,114	14	148
	1974			
V. Georgetown University Hospital	1972	15,300 2/	93	322
	1973	15,572	83	377
	1974	15,610	81	327
VI. Holy Cross Hospital	1972	19,046	11	18
	1973	19,190	12	32
	1974	19,815	14	10
VII. Greater South East Hospital	1971	15,847	6	63
	1972	19,530	26	78
	1973	18,919	17	82
	1974	18,287	14	39

1/ Maintains statistics on fiscal rather than calendar year
2/ Estimated admissions for 1972

Table 2-2
Coverage Comparisons: RTI National Dialysis Registry and California Kidney Disease Information System Data on Dialysis and Transplants, ASC Organ Transplant Registry and CKDIS

	Numbers Entering Dialysis in Year Given			Numbers Transplanted In Year Given				
	(1) RTI	(2) CKDIS	(1)/(2)	(3) RTI	(4) CKDIS	(3)/(4)	(5) ACS	(5)/(4)
1972	458	543	.84	109	289	.37	186	.64
1973	427	875	.49	91	284	.32	184	.65

Sources:

RTI Computer Files
CKDIS Tables
"Chronic Hemodialysis Patients..." October 30, 1974

"Transplant Statistics, 1972, 1973, 1974"
ACS/NIH Computer Files

CHAPTER THREE

III. PARAMETER ESTIMATION

The basic transition probabilities for the disease treatment section of the matrix were estimated from patient histories in the RTI and ACS files. Parameters related to the "well" state (state 1), specifically the probability of remaining well or of death from the well state, were estimated from regional population data collected by the Census Bureau and the National Center for Health Statistics.

Two approaches to parameter estimation of the transition probabilities were used. Classical maximum likelihood estimates were computed to bring out the structural characteristics of the system and to provide a basis for arguing the reasonableness of a Markov formulation. A technical discussion of the maximum likelihood estimation assumptions appears in Appendix (B). Then, for the purpose of forecasting, the parameters were re-estimated using Bayes' theorem to build in prior information. Staff members felt that, given the sample size available, Bayesian estimates, though not superior structually to MLE, might yield more reliable forecasts. A discussion of Bayes' technique appears in Appendix (C).

Time dependent and homogeneous estimates were computed using both classical and Bayesian formulas, for subsets of the population classified by age, region and sex. Regions have been identified in Chapter One. The age classification is comparable to usage in other studies and in Census publications: Group 1, 0-14 years, Group 2, 15-44 years, Group 3, 45-64 years and Group 4, 65 plus years.

A. Homogeneous Transition Probabilities From Daily ACS Data

Because of inadequate information on non-transplants, the ACS

data have not been used in forecasting. However, since it is believed that the quality of data from this source is superior, readers interested in results from ACS maximum likelihood estimates are referred to Tables 3-1 through 3-3 for estimated transition probabilities. Note the absence of state 1 in these matrixes. We saw no reason to build in a "well" population estimate, since there was no way of determining from what state patients came when undergoing transplant surgery.

Theoretically, the day-by-day information available for ACS patients should permit a more rigorous application of the Markov model to these data. A daily unit time period effectively excludes the possibility of multiple events. Unfortunately, the limitations imposed on these data by the methods of record keeping discussed above tend to counteract the advantages of detail.

Estimates were based on ACS patient histories over the 31 days of January, 1973. We chose this month to represent recent technology and practice, and to permit comparison with observations from the RTI sample. Thus limited, it is important to note that, whatever prior expectations one might have about parameters, there is an imbalance in the estimates that precludes serious structural analysis. Most patients enter the system either as stable recipients of prior transplants or as post-transplant dialysis patients. Moreover, they tend to remain in these states over the period of observation.[4]

4 It might be argued that increasing the period of observation beyond one month would increase the likelihood of observing transitions in now-empty states. We considered sampling the ACS data and computing daily probabilities over the year 1973. Empirical holding times for the sample are long enough, however, to limit the probable success of this approach. Moreover, one must always keep in mind the fundamental data limitations we encountered. For example, more information on transplantation could only cover re-transplants, because we have no information of states prior to the first transplant. For the computations made, we assumed all patients with transplants in

An expanded time frame could improve considerably any potential survival analysis based on these data, by filling in gaps in mortality transitions (into state 7). Fortunately, an ACS publication, the Transplant Fact Book does a fairly thorough job of estimating survival rates for patients fitting a variety of categories. (REF 2)

In sum, we caution the reader to avoid drawing firm conclusions about regional, age or sex-related differences in transition probabilities from these data. Whereas an expanded time frame might add information on transitions, data limitations restrict the value of this exercise. No time frame is sufficient, however, to make use of the ACS data base, in current form, for forecasting.

B. Homogeneous Transition Probabilities From Monthly RTI Data

Parameter estimates for the RTI data were computed in two stages. Sample data from January, 1972 through December, 1973 were used. Since transition points in the RTI data base were identified by month, we had to sacrifice theoretical rigor (the preferred daily transition probability) in the interests of analyzing a data base with fairly broad coverage of the treatment system. Of course, the possibility of multiple transitions within a month exists. For consistency, we adopted the following coding conventions:

1. A month in which a transplant occurred was identified as such, though, of course, the precise transition normally involves dialysis-transplant-well (or return to dialysis), within a three day period.

&t/January, 1973 entered from dialysis (state 3). This assumption is plausible when the maximum time in dialysis prior to transplant cannot exceed 30 days. It is much less plausible for a transplant in June, let us say, before which a patient may have been well through March and on dialysis thereafter, until the day of transplant.

2. Multiple transplants in a given month were treated as a single transplant, leading inevitably to an underestimate of the transplant -- transplant transition probabilities.

3. Month of death: Death is assumed to have occurred on day one of this month, causing the month to be identified with the death state.

Tables 3-4 through 3-7 give the results of estimation from the 25% sample, and exclude estimates of well population flows; thus, only states 2 through 7 are included. Tables 3-5 through 3-7 give results by sex groupings. Tables 3-8 through 3-10 show MLE matrixes inflated to population size. Appendix D discusses the estimation of parameters related to the well state (state 1). For the latter analysis, it seemed advisable to drop the sex category in order to strengthen the reliability of our estimates. However, certain differences in estimates by sex do appear, and should be mentioned in order to suggest the possible costs of aggregation.

Sex differences in the propensity to remain on institutional dialysis are reasonably consistent (See Tables 3-5 through 3-7). Except for the older New England group, men are more likely to move out of institutional dialysis than are women.[5] With the exception of younger Californians, there appears to be a tendency for relatively larger numbers of men to move from institutional to home dialysis. The selection process may, however, more effectively screen females unlikely to succeed at home dialysis. Except for older persons in

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4ctFurther, dialysis from this sample can only be defined as post-transplant dialysis. Longer periods of observation will not increase information about chronic maintenance dialysis prior to transplant or as a choice of treatment for patients unsuited for transplant.

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5 The width of the sex difference is greatest for both age groups in New England, but small sample size seriously compromises the reliability of these results (note the absence of observations for women moving from institutional dialysis to home dialysis and death, and home dialysis to death.)

the South, the death rate for men on home dialysis exceeds that for women. Death for those on institutional hemodialysis follows no obvious pattern by sex. The total probability of death out of dialysis is lower for women in all classes except older New Englanders and Southerners.

C. Age Differences in Transition Probabilities

Age has been retained as an important structural variable throughout the analysis. Table 3-13 through 3-15 present maximum likelihood estimates for the 4 age categories, by region. Some experimental aggregation was tried, lumping age groups 1 and 2, and 3 and 4, as shown in Tables 3-10 and 3-11.

The effect of age moves in the expected directions, as shown in Table 3-10 through 3-17. Comparing groups 2 and 3, older patients are more likely to remain on institutional dialysis than younger patients. Older patients are less likely to move into home dialysis than younger patients, but, for those few older patients selected for home dialysis, survival chances are greater than for the younger group (See Ghantous for a discussion of this phenomenon).[1] Age groups one and four are sparsely populated, and thus difficult to interpret. It seems generally true, however, that very young and very old patients rarely have the option of home dialysis or of institutional peritoneal dialysis.

To test statistically the value of a 4-way age breakdown, chi-square statistics were computed to test the null hypothesis that pooled age classes (1+2 and 3+4) yield probabilities insignificantly

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different from those of the unpooled classifications. The results appear in Table 3-18. Tests were made on states 2-6 only, since the concern for differences affecting the disease-treatment subsystem of our model. The effect of relative class size appears in the results. Classes 2 and 3, with large patient populations and high rates of activity, generate statistics strongly suggesting the significance of age. Age groups 1 and 4, with small populations and fairly restricted activity tend, on the other hand, to support the null hypothesis of no age impact. In general, we are confident that age does make a difference to the analysis and forecasting process. Finally, death rates for those on institutional dialysis clearly increase with age.

D. Tests of Homogeneity

Tables shown in this report include, for the sake of brevity, only the homogeneous Markov matrixes. Of course, the assumption of homegeneity is crucial in judging the value of this model for forecasting. We ran chi-square tests (described in Appendix E) to check the reasonableness of assuming the existence of time-independent parameters. These tests were applied both to maximum likelihood estimates and to the Bayesian estimates. It should be noted, however, that strong homogeneity of the Bayesian probabilities can be presumed, since the introduction of prior information tends to smooth the time dependent estimates. For probability parameters assumed by theory to be positive, a Bayesian estimate will always be positive. The maximum likelihood estimate depends on an empirical sample, however, and specific probability values can appear as zeros, however unreasonable this might seem on theoretical grounds. Tables 3-19

and 3-20 present the chi-square statistics for tests of homogeneity of the transition probabilities over time. The results of these tests agree with Cooper's general observation that most transition probabilities observed in the kidney disease-treatment system are reasonably stable through time, with the exception of institutional dialysis (state 5).[1] Three out of seven MLE statistics are homogeneous for the "stable" and "home" dialysis states (states 2 and 3) and all of the Bayesian estimates are homogeneous for these states. All statistics for state 4 (peritoneal dialysis) and state 6 (transplant) show homogeneity.

More broadly, one can test the hypothesis that $P_{ij}(t) = P_{ij}$ for all i simultaneously. Table 3-20, column 7 present the results of this exercise. With more degrees of freedom available, the simultaneous χ^2 for Boston (Region I) supports the homogeneity hypothesis for all age groups with both MLE and Bayesian estimates. However, the large and active age groups 2 and 3 for the South and California confirm the null hypothesis through the Bayesian but not the MLE estimates, thus leaving open the question of stability. But one is provided with some indication of <u>relative</u> stability across age groups and states. On the basis of these tests, one feels justified in talking about <u>a</u> Markov matrix, for appropriate age-sex-region classifications, rather than 24 separate time dependent matrixes.

E. Structure of the System

One can make use of the matrix (MLE) of pooled estimates in Table 3-8 to discuss the general structure of the disease-treatment system. Later, the study will look at the impact of age and region

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on parameter estimates, using appropriate disaggregated matrixes.

1. Zero Elements

Several elements in the pooled matrix are zero, and it would be well to distinguish those that are empty because the parameters in question do not exist from those that are empty because our sample lacked the needed observations. Transitions P_{21}, P_{31},....P_{61} are assumed impossible; that is chronic kidney patients can never become "well" again, whatever treatment they might receive Of course, P_{71}, P_{72}....P_{76} cannot occur because 7 (death) is an absorbing state. (P_{77} will then always equal 1.00, or death in one month is followed by a perfect probability of death in the next month). We assume that P_{12} will be equal to zero, since to move to a Stable (2) state, one must have received a successful transplant in the preceeding month. By the same logic, P_{32}, P_{42} and P_{52} are impossible. A patient cannot move directly from any form of dialysis to stability, a state which implies the need for dialysis has been removed. (We encountered records suggesting such transitions, but conclude that they represent the mistaken entry of acute patients into a population of chronic cases. They have been excluded from this analysis). A transition from "well" to "transplant" (P_{16}) in the space of 2 months is logically possible, and we encountered a few cases that followed this track. Of course, the true (but submerged) sequence probably involved a spell of pre-transplant dialysis. But since the analytical time unit must remain a month, we must accept the less precise P_{16} pattern that our data allow.

Several elements in this (and subsequent) matrixes are estimated to equal zero, though we must assume that the true parameters are positive. The Bayesian matrix in Table 3-8 points out the cells that should be filled (and are filled, via the prior distribution assumed for the Bayesian estimates). It should be noted that P_{13}, P_{14} and P_{16} transitions from well to home and peritoneal dialysis, and to transplantation, are empty in the MLE matrix because, though transitions occurred, their small numbers were overwhelmed by the weight of P_{11} and P_{17} transitions. Thus they yield no positive probabilities as a result of rounding by the computer program. The Bayesian estimates solved this problem for P_{13} and P_{14}, but not for P_{16}.

Transitions from the stable state to peritoneal dialysis and to transplant (P_{24}, P_{26}) are computed to be zero, but cannot be rejected on structural grounds. It is particularly unfortunate that a good monthly estimate of second and third transplant probabilities was not possible. Of course a P_{26} probability exists over longer periods, by virtue of passage through intermediate states, such as institutional hemodialysis.

Peritoneal dialysis, a sparsely populated state with very limited activity, computes zeroes for P_{45} (peritoneal to institutional hemodialysis) and P_{64} (transplant to peritoneal dialysis). We have no basis for assuming these parameters do not exist.

Transition from transplant to home dialysis (P_{63}), which here is estimated to be zero, is a logical possibility. Even though home dialysis requires a training period during which the patient is dialized at an institution, the positive probability of moving from home

dialysis to transplant (P_{36}) indicates that a pool of home-trained individuals with transplants exists. Presumably, a malfunction could return such a patient either to home or to institutional dialysis without further training.

Finally, it is quite clear that P_{66}, back-to-back transplants, should be positive, though our sample data furnish no estimate. Much of the weakness in estimation of state 6 probabilities might be overcome by better basic "population" figures. As we mentioned above, RTI's coverage of transplant activity is poor.

2. Diagonal Elements

Transition probabilities along the diagonal of the matrix indicate the average one-month tendency to remain in states of the system. States 1, 2, 3 and 5 tend to hold large numbers of their occupants from month to month. On average, 98 out of 100 patients who are stable (state 2) this month will be stable next month. Stable and home dialysis are more likly to retain patients from month to month than is State 5, institutional hemodialysis. State 5 acts as a feeder for states 3 and 6, home dialysis and transplant, and indirectly for state 2, through the transplant state.

State 4, peritoneal dialysis, appears to serve as a feeder to more permanent states, particularly state 3 (home dialysis) and state 6, transplant. Eighty-six out of 100 patients remain on peritoneal dialysis from month to month. Of course, "holding" in state 6 (transplant) is a concept with little meaning. We have discussed the absence of data to estimate P_{66} above. Though doubting the hypothesis

that $P_{66} = 0$, we feel nonetheless that transplant patients are shown held in a successful post-transplant state by P_{22}. A combination of P_{62} and P_{22}, then, accomplishes the description of immediate and longer term transplant function that we associated with a diagonal element.

3. The Dialysis Subsystem

If we separate out a 3 x 3 submatrix for states 3-5, we have isolated a dialysis subsystem that highlights some interesting points. First, dialysis of any kind is a persistent state for those who have entered the subsystem. Ninety-eight out of 100 patients beginning on home dialysis will be on some form of dialysis next month where:

$$P_3 \text{ (dialysis)} = \sum_{j=3}^{5} P_{3j}$$

Ninety-seven of 100 on institutional hemodialysis will stay in the subsystem and 93 of 100 on peritoneal dialysis will be retained on some form of dialysis next month.

It is also clear that over time, the balance of flows within the subsystem increases state 3, home dialysis, at the expense of state 4 and 5, since:

$$P_{53} > P_{35}$$

and $P_{43} > P_{34}$

Thus if 100 individuals entered each dialysis state (3 through 5) at month 1 (and zero individuals in all other states) by month 2, allowing for subtractions by death and transplantation, 106 patients would be on home dialysis, 86 on peritoneal dialysis and 96 on institutional hemodialysis.

By adding states 2 (stable) and 6 (transplant) to our 3 x 3 matrix of dialysis states, a chronic treatment subsystem may be constructed. As might be expected, patients on institutional hemodialysis and peritoneal dialysis have a one-month probability of transplantation greater than that for home dialysis patients. Of 100 patients, 14 from state 4 and 13 from state 5 will be transplanted in the transition month. Only one home dialysis patient will receive a transplant.

The initial success rates for transplants are indicated by the transition probabilities in row 6. Eighty-three of 100 transplants are initially successful, 16 of 100 malfunction without fatality (and according to this model return for the month, at least, to institutional dialysis), and one of 100 patients dies immediately following transplant.

For those who have enjoyed a functioning transplant for at least one month (state 2), there is a 11/1000 probability that a non-fatal malfunction will be suffered. Again, the dialysis treatment preferred for patients with failed transplants is institutional hemodialysis. Nine of the failures will enter state 5, and two will enter state 3.

4. Death Rates

Monthly death rates may be read from the estimate in column 7 of each matrix. The "well population" death rate was estimated, as described in Appendix (D) from published sources, and corrected for government figures on death for chronic kidney failure. Death rates from the disease-treatment system (P_{27}, $P_{37}...P_{67}$) were estimated from sample data.

Our estimates suggest that the morality rate for all forms of dialysis exceeds that for either immediate post-transplant mortality (P_{67}) or death from the stable state (P_{27}). It should be noted that small numbers limit the statistical reliability of P_{47}, death from peritoneal dialysis. We have no reason to believe, a priori, that the death rate for peritoneal dialysis is five times the death rate for institutional hemodialysis. Home hemodialysis, with a death rate of 9/1000 and institutional hemodialysis, 11/1000, show mortality rates almost double those for transplant and stable states (6/1000 and 5/1000 respectively).

In summarizing the discussion, it should be remembered that substantive conclusions about the relative size of certain parameters may change when subjected to age or regional disaggregation. Certain broad points seem clear, however:

1. Many of the system parameters cannot be estimated using MLE techniques on existing data.
2. The system exhibits a propensity to stability in holding patterns over sizeable time periods, as indicated by high values for the diagonal estimates.
3. States 2 (transplant) and 3 (home dialysis) tend on balance to accumulate and hold patients, whereas states 4 (peritoneal dialysis) and 5 (institutional hemodialysis) act in part to move patients into these holding states.
4. Mortality rates associated with dialysis exceed mortality rates associated with transplantation by any measure.

We have designed the data sampling and analytical base of this project to produce a regional forecasting model. It would be useful to examine what inter-regional differences appear in the parameter estimates.

F. Regional Differences in Transition Probabilities

1. zero Elements:

Regionalization should have no effect on the arguments presented above about logically zero elements. Note that Region 1, Boston megalopolis, has more zero cells in its matrix than Region 2 (Southern states) and Region 3 (California),(see Table 3-9.) One is inclined to attribute this to a relatively small number of observations for Region 1 (124 compared to 294 for Region 2 and 420 for Region 3). Certainly, Region 1's diversity of treatment options rivals that of the other regions.

Region 3 recorded transitions sufficient to compute positive values for P_{13}, P_{14} and P_{16}. However, once again the probabilities were too small to meet the cut-off rules of the computation procedure, and were accordingly dropped in the MLE estimates.

2. Diagonal Elements

With the exception of state 4 (peritoneal dialysis), regional differences in diagonal elements are not great. The problems posed by limited observations on state 4 are, of course, magnified when the data are disaggregated.

Boston and California holding probabilities appear to be uniformly larger than the average (compare with Table 3-8), whereas the South shows diagonal elements smaller than the average. This means the average patient in the Southern system is more likely to move between states in a month than is a patient in the other systems. To help explain this result, one must examine other characteristics of the matrixes, in particular the nature of the off-diagonal transitions.

3. Dialysis Subsystem

The 3 x 3 matrix of dialysis states again highlights contrasts between the data for Region 2 and those for Regions 1 and 3.

Southern patients have a probability of moving from state 5 (institutional dialysis) to state 3 (home dialysis) in a month that is considerably higher than that for Boston or California. Twenty-two/thousand make this transition in the South, compared to 3/1000 in Boston. This relatively heavy reliance on home dialysis in the South confirms our earlier impressions of regional difference in treatment patterns.

Chances of leaving the dialysis subsystem are about equal across regions, if one excludes state 4. It is unrealistic to assume, as the estimates suggest for state 4 in California and Boston, that all patients beginning in peritoneal dialysis are in some type of dialysis the following month. Of patients beginning in home dialysis, 99/100 in Boston and California remain on some type of dialysis the next month, compared to 98/100 for the South. For patients beginning on institutional dialysis the rates are 98/100 for Boston and California, and 97/100 for the South.

4. The Dialysis - Transplant Subsystem

In general, the rate at which dialysis patients are transplanted is higher in Boston and the South than in California. Boston's transplant rate out of institutional dialysis is 15/1000, the highest from any dialysis category (if transplant out of peritoneal dialysis in the South is excluded). The Southern rate, 14/1000 exceeds California (12/1000), though the discrepancy is not great.

As we mentioned above, transplants are more probable for patients on institutional hemodialysis than for those on home dialysis. The figures for each of the three regions bear out this argument. The South, with 10/1000, has the highest home dialysis to transplant rate, closely matched with Boston's 9/1000. California's 6/1000 suggests a long-term treatment option than prevails in the other two regions.

Once transplanted, a Southern patient seems to risk a relatively high immediate failure rate (transplant to institutional hemodialysis P_{65}) as well as a high rate of failure from the stable state ($P_{23} + P_{24} + P_{25}$). Though there are no observations from the Boston data, and one must therefore suspend judgment on the value of P_{65} for Region 1, one can observe that 30 out of 100 transplant patients immediately return to dialysis, compared to 11 out of 100 in California. Fourteen of 1000 functioning transplants (a patient in state 2 for at least one month) fail each month in the South, compared to 9 of 1000 failures in Boston and California.

5. Death Rates

Southern death rates from disease treatment states exceed those in other regions. In the South, 11 of 1000 patients with functioning transplants die each month. By comparison, only 5 of 1000 die in the Boston region, and 2 of 1000 die in California. The same discrepancy exists for home dialysis. Thirteen of 1000 Southern home dialysis patients die each month, compared to 9 of 1000 in California and 2 of 1000 for Boston. Death from institutional hemodialysis follows a similar pattern; 14/1000 for the South, 12/1000 for California and 7/1000 for Boston.

It is interesting to note that though the South shows death rates from kidney disease treatment states higher than those in the other regions, the South's non-kidney related over-all death rate is the lowest of the three. The South's average monthly death rate /100,000 is 64.41, compared to California, 67.78 and Boston, 127.97. Thus the phenomenon of higher kidney-related mortality cannot be explained by purely demographic and non-treatment related factors.

In summary, the South appears to differ from Boston and California in several ways:

(1) A relatively high probability of channeling patients into home dialysis <u>but</u> a relatively high probability of selecting home dialysis patients for transplant.

(2) A relatively high failure rate for transplants.

(3) A relatively high death rate from dialysis and stable transplant states, despite a relatively low death rate from causes unrelated to kidney disease.

It should be remembered that this model has little explanatory power, and that we are thus unable to point out why the South differs so greatly from the other regions in these ways. However, since age structure across regions affects death rates as well as success in kidney treatment, one should examine the age specific estimates of transition probabilities that form the core of the forecasting model.

G. Impact of Age on Transition Probabilities Age Structure of the Regional Populations

Table 1-1 presents a breakdown of regional population estimates for 1972 and 1973, in the four age classes used in this study. The Boston megalopolis stands out as an older population than those of the Southern states and California. Roughly 67% of the population in Boston were under 45 years of age in 1972, compared to 72% in the South and 71% in California. More striking, perhaps, is the fact that 13% of Boston's population are over 65 years, compared to 9% for both the South and California. Thus age structure can be offered as a partial explanation for the relatively high death rate in Boston (twice the death rates in the South and in California). These demographic facts do not, however, help to explain the fact that the South shows relatively high rates of kidney disease related death, since one would normally assume that death rates for older populations will be higher for chronic disease of any kind than those for younger populations.

To examine the region - age differences in the way that the kidney disease treatment system operates, we constructed Tables 3-10 and 3-15, which use pooled age group information to test the age breakdown of computed transition probabilities. We pooled age groups 1 and 2, and 3 and 4, because our 4-way age classification yielded many zeroes and sparsely populated cells. In effect, then, we are comparing the population under 45 (the "young" group) with the population 45 and over (the "old" group). Peritoneal and home hemodialysis, as well as transplantation, have not been widely used in treating very young and very old patients. There is evidence that medical practice is moving toward more liberal age standards for accepting dialysis and transplant patients.

Entries in Table 3-21 are ratios of transition probabilities for the young group to the sum of the probabilities of both young and old groups. Thus the entry in row 1, column 5 would be

$$\frac{P_{15}^{(1+2)}}{P_{15}^{(1+2)} + P_{15}^{(3+4)}}$$

and can be interpreted thus: if 1000 individuals entered institutional hemodialysis from the well state in Region 1 during a month, 229 of them would be from the young group and the rest from the older group. This figure suggests an age mix for this particular transition which is heavily weighted toward old people.

1. <u>Diagonal Elements</u>

Apparently age has little effect on the propensity to remain stable after a transplant (P_{22}) though younger patients have a slight edge in Regions 1 and 2 (503 out of 1000 for the Boston megalopolis and 506 out of 1000 for the rural Southern states.

This parity remains for the principal diagonal elements of home and institutional dialysis in Region 1. However, it appears that young patients are somewhat less likely to remain on dialysis in Regions 2 and 3 than are older patients; for home dialysis, 499 young Southern patients out of 1000 and 497 young Californians will stay, and for institutional hemodialysis, 497 young Southerners and 495 young Californians will stay.

2. <u>The Dialysis - Transplant Subsystem</u>

As above, age differentiates the estimates of the Boston region from the South and California in the dialysis-transplant subsystem of the matrix.

Young patients are less likely to move into home dialysis from institutional hemodialysis than are old patients in Boston; 421 of 1000 who make this transition are in the young group. On the other hand, the Southern home dialysis candidate is somewhat more likely to be young (583 of 1000), as is the Californian (595 of 1000).

Of those home dialysis patients receiving transplants, a sizeable majority in the South and in California are young. For the South 717 of 1000 home dialysis transplant transitions involve young patients, and for California, 833 of 1000. Again the contrast with Boston is striking. Only 203 of 1000 home dialysis patients who are transplanted will be young, in the Boston region. For transplantation out of the institutional hemodialysis state, it is clear that young patients predominate in all three regions, but the margin is small in the Boston region. Only 522 of 1000 transplant recipients who came from institutional dialysis in

Boston will be young, compared to 792 from in the South and 849 of 1000 in California.

3. Death Rates

It was commented earlier that the death rate for young home dialysis patients appears to be higher than that for older home dialysis patients. Table 3-19 supports this comment for each of the three regions. All deaths from home dialysis would be among the young for Boston, compared to 280 of 1000 for stable transplant patients and 195 of 1000 for patients on institutional dialysis. Five hundred twenty of 1000 home dialysis deaths in the South will be from the younger age group, compared to 466 of 1000 for stable transplant and 326 of 1000 for institutional hemodialysis. And 554 of 1000 home dialysis deaths in California will be from the young patient population, compared to 464 of 1000 for stable transplant and 417 of 1000 for institutional dialysis.

As these figures indicate, the discrepancies in death rates by age are greatest for the Boston megalopolis, being very low for young patients in states other than home dialysis, and unnaturally high for home dialysis. The South-California figures do not differ greatly, though the relative age mix appears somewhat younger in the California death rates (with the exception of death from the stable transplant state, where the difference is a trivial .002).

From a slightly different perspective, the data from Tables 3-10 and 3-11 show that inter-regional differences in death rates vary by age group. Southern death rates exceed Boston death rates by factors of 3 or 4 in the young age group, but only by factors of 1.5 to 2 in the older age group. The discrepancies between the

South and California are less pronounced. The ratio:

$$\frac{\text{Southern death rate}}{\text{California death rate}}$$

is 4.80 for the young group and 4.75 for the old group, for stable transplant patients. For home dialysis patients, higher southern rates persist but the age pattern is reversed; 1.30 for the young patients and 1.50 for old patients. Only in institutional hemodialysis do Southern rates fall below California rates. Here too, however, the fundamental tendency for relative death rates to work against young Southerners reasserts itself. The ratio is .97 for the young age group, and .26 for the old age group.

H. Summary

Kidney disease treatment transitions in the three regions of this study are affected by patient age in diverse ways. The relative youth of Southern and California populations is mirrored in the system in two areas:

1. The rural Southern states and California are more likely to move young patients to home dialysis than is Region 1. Boston's treatment system seems more oriented toward providing a diversity of treatment options to its fundamentally older population.
2. Southern death rates tend to exceed death rates in other regions, and the discrepancy is widest in the young age group between South (with the most youthful regional population) and the Boston megalopolis (with the oldest regional population).

I. Incidence of Chronic Kidney Disease

By combining the regional population estimates computed for the forecasting model with observations from RTI data on the numbers entering chronic kidney disease treatment, it is possible to estimate the incidence of treated chronic kidney disease, by region and by age. Table 23 presents the results of these computations.

Incidence here is computed to be the ratio of:

> The sum of all transitions from the well state into states 3 - 5 (dialysis) and 6 (transplant) for a given year (by age, region): to total estimated population (by age, region, or total) at mid-year.

Figures were developed for the data pooled (over region and age group), and for pooled age groups (1 and 2) and (3 and 4), by region.

Overall incidence for 1972 and 1973, 24 and 22/million, seems very low compared to incidence estimates generated by others studies. Incidence rates have been estimated to be as low as 20/million and as high as 70/million. (For a discussion of estimates in the literature, see Cooper REF 92.)

Age-region specific incidence rates show Boston's to be the highest incidence for both age groups. California's incidence for the younger age group is the lowest of the three, but the South shows the lowest incidence of treated kidney disease for the older age group.

J. Recapitulation

In this discussion of parameter estimates, we have tried to point out some general structural characteristics of the kidney

disease treatment system that the model reflects. We have also brought out the importance of regional factors that affect the way the model operates. The section on age factors was meant to add some depth to the regional discussion. We felt uneasy about facile explanations of phenomena; with the data available, it would be unwise to attribute the relatively high Southern death rates to treatment practices oriented toward a relatively young population. Our information on structural and institutional details would be insufficient for more than the largely descriptive statement made above. These regional differences bear further investigation, a project beyond the scope of this study.

Table 3-1
ACS Homogeneous Markov
Matrixes (Daily Probabilities)
Region 1 Boston Megalopolis

	Male					Female				
	2	3	4	5	6	2	3	4	5	6
Age 15-44 M: (N=171) F: (N=71)										
2	1.0000					1.0000				
3		.9987		.0013			1.0000			
4										
5										
6										
Age 45-64 M: (N=73) F: (N=36)										
2	.9995	.0005				.9990				.0010
3		1.0000					1.0000			
4										
5										
6										1.0000

Source: American College of Surgeons/National Institutes of Health Organ Transplant Registry Files

Note: Age groups 0-14 and 65 + were omitted from this table because of insufficient numbers of reporting units.

States:

2 Stable
3 Dialysis
4 Live Donor Transplant
5 Cadaver Donor Transplant
6 Death

Table 3-2
ACS Homogeneous Markov
Matrixes (Daily Probabilities)
Region 2 (South)

	Male					Female				
	2	3	4	5	6	2	3	4	5	6
Age 15-44 M: (N=161) F: (N=70)										
2	.9988	.0009			.0002	.9985	.0015			
3		.9967		.0033			1.0000			
4										
5		1.0000								
6					1.0000					
Age 45-64 M: (N=44) F: (N=14)										
2	.9972				.0028	1.0000				
3		1.0000					1.0000			
4										
5										
6					1.0000					

States

2 Stable
3 Dialysis
4 Live Donor Transplant
5 Cadaver Doner Transplant
6 Death

Source: As in Table 3-1

Table 3-3
ACS Homogeneous Markov
Matrixes (Daily Probabilities)
Region 3 California

	Male					Female				
	2	3	4	5	6	2	3	4	5	6
Age 15-44 M: (N=189) F: (N=143)										
2	.9998	.0002				.9997	.0003			
3		.9981		.0019			1.0000			
4										
5										
6										
Age 45-64 M: (N=38) F: (N=39)										
2	1.0000					1.0000				
3		1.0000					.9945			.0055
4										
5										1.0000
6										

States

2 Stable
3 Dialysis
4 Live Doner Transplant
5 Cadaver Transplant
6 Death

Source: As in Table 3-1

Table 3-4
Homogeneous Markov Matrixes
(Monthly Probabilities)
Region 1 - Boston Megalopolis

Receiving States

Sending States	1 Well	2 Stable	3 Home Dialysis	4 Peritoneal Dialysis	5 Institutional Hemodialysis	6 Transplant	7 Death
1							
2		.9738			.0164		.0098
3			.9823			.0141	.0035
4			.1000	.9000			
5			.0035		.9705	.0165	.0095
6		1.0000					1.0000
7							

Region 2 - Rural Southern States

	1	2	3	4	5	6	7
1							
2		.9922	.0023		.0019		.0035
3			.9774	.0008		.0100	.0117
4			.0323	.8065		.0323	.1290
5			.0217	.0005	.9490	.0142	.0147
6		.9546			.0455		
7							1.0000

Region 3 - California

	1	2	3	4	5	6	7
1							
2		.9876			.0093		.0031
3			.9834		.0007	.0060	.0100
4			.2143	.7857			
5			.0074		.9690	.0113	.0124
6		.8431			.1373		.0196
7							1.0000

Source: RTI National Dialysis Registry Data
Computed from raw data by Roy Littlejohn Associates

Table 3-5
Region

Matrices, by Sex and Age

Boston Megalopolis

Male - Ages 15 - 44

	1	2	3	4	5	6	7
1							
2		.9919			.0081		
3			.9722			.0139	.0139
4							
5			.0060		.9642	.0239	.0060
6		1.0000					
7							1.0000

Male - Ages 45 - 64

	1	2	3	4	5	6	7
1							
2		.9540			.0230		.0230
3			.9748			.0252	
4			.1000	.9000			
5			.0050		.9700	.0150	.0100
6		1.0000					
7							1.0000

Female - Ages 15 - 44

	1	2	3	4	5	6	7
1							
2		.9639			.0182		.0182
3			1.0000				
4							
5					.9899	.0101	
6		1.0000					
7							1.0000

Female - Ages 45 - 64

	1	2	3	4	5	6	7
1							
2		.9474			.0526		
3							
4							
5					.9600	.0160	.0240
6		1.0000					
7							1.0000

Source RTI National Dialysis Registry Data
Computed from raw data by Roy Littlejohn Associates, Inc.
For list of states, see Table 3-4.

Table 3-6
Region 2
Matrices, by Sex and Age
South

Male - Ages 15 - 44

	1	2	3	4	5	6	7
1							
2		.9747	.0051		.0101		.0101
3			.9769			.0096	.0135
4			.5000			.5000	
5			.0315	.0016	.9339	.0205	.0126
6		.9474			.0526		
7							1.0000

Male - Ages 45 - 64

	1	2	3	4	5	6	7
1							
2		.9760	.0096				.0144
3		.0025	.9801	.0025		.0074	.0074
4				.8889			.1111
5		.0042	.0198		.9518	.0071	.0170
6		.9000			.1000		
7							1.0000

Female - Ages 15 - 44

	1	2	3	4	5	6	7
1							
2		.9524	.0190		.0095		.0190
3			.9655			.0230	.1115
4				.5000			.5000
5			.0203		.9481	.0248	.0068
6		1.0000					
7							1.0000

Female - Ages 45 - 64

	1	2	3	4	5	6	7
1							
2		1.0000					
3			.9881				.0119
4							
5			.0093		.9719		.0187
6							
7							1.0000

Source: As in Table 3-5

Table 3-7
Region 3
Matrices, by Sex and Age
California

Male - Ages 15 - 44

	1	2	3	4	5	6	7
1							
2		.9803			.0172		.0025
3			.9660			.0154	.0185
4							
5		.0011	.0080		.9588	.0252	.0069
6		.7778			.2222		
7							

Male - Ages 45 - 64

	1	2	3	4	5	6	7
1							
2		.9764			.0236		
3			.9844			.0016	.0140
4			.2222	.7778			
5			.0067		.9725	.0041	.0165
6		1.0000					
7							1.0000

Female - Ages 15 - 44

	1	2	3	4	5	6	7
1							
2		.9937			.0021		.0042
3			.9881			.0119	
4							
5			.0130		.95595	.0146	.0130
6		1.0000					
7							

Female - Ages 45 - 64

	1	2	3	4	5	6	7
1							
2		.9937					.0063
3			.9942		.0029	.0029	
4			.2000	.8000			
5			.0051		.9809	.0051	.0089
6		.6000			.2000		.2000
7							1.0000

Source: As in Table 3-5

Tabl[illegible]

Homogeneous [illegible]E Markov
Matrixes (Monthly Probabilities):
Pooled Age, Sex: 3 Regions

Region 1: Boston Megalopolis

	1	2	3	4	5	6	7
1	.9987169				.0000034		.0012797
2		.9861111			.0086806		.0052083
3			.9893390			.0085288	.0021322
4			.1000000	.9000000			
5			.0018215		.9769277	.0145719	.0066789
6		1.0000000					
7							1.0000000

Region 2: South

	1	2	3	4	5	6	7
1	.9993542		.0000001	.0000001	.0000016		.0006441
2		.9742647	.0073507		.0073529		.0110294
3			.9770370	.0207407		.0096296	.0125926
4			.0200000	.880000		.0200000	.0800000
5			.0218467	.0004122	.9505359	.0136026	.0136026
6		.7031250			.2968750		
7							1.0000000

Region 3: California

	1	2	3	4	5	6	7
1	.9993203				.0000019		.0006778
2		.9886942			.0090447		.0022612
3			.9843297		.0005804	.0063842	.0087057
4			.3793103	.6206892			
5			.0033784		.9729730	.0119369	.0117117
6		.8750000			.1093750		.0156250
7							1.0000000

Source: As in Table 3-4

Table 3-10
RTI Homogeneous MLE Markov
Matrixes (Monthly Probabilities):
Pooled Age Groups (1 & 2): 3 Regions

Region 1: Boston Megalopolis

	1	2	3	4	5	6	7
1	.9998963				.0000019		.0001099
2		.9907407			.0061728		.0030864
3			.9914163			.0042918	.0042918
4							
5			.0025349		.9797212	.0152091	.0025349
6		1.0000000					
7							1.0000000

Region 2: South

	1	2	3	4	5	6	7
1	.9998640		.0000001		.0000013		.0001366
2		.9737762	.0069930		.0087413		.0104895
3			.9739583			.0130208	.0130208
4			.2500000	.2500000		.2500000	.2500000
5			.0250760	.0007598	.9445289	.0205167	.0091185
6		.9459459			.0540541		
7							1.0000000

Region 3: California

	1	2	3	4	5	6	7
1	.9998902				.0000010		.0001032
2		.9890750			.0087400		.0021850
3			.9767055			.0133111	.0099834
4			.0083149		.9589800	.0232816	.0094235
5							
6		.8800000			.1200000		
7							1.0000000

Source: As in Table 3-4

Table 3-11
RTI Homogeneous MLE Markov
Matrixes (Monthly Probabilities):
Pooled Age Groups (3 & 4): 3 Regions

Region 1: Boston Megalopolis

	1	2	3	4	5	6	7
1	.9963775				.0000064	.0000001	.0037160
2		.9801587			.0119048		.0079365
3			.9831224			.0168776	
4			.1000000	.9000000			
5			.0034884		.9720930	.0139535	.0104651
6		1.0000000					
7							1.0000000

Region 2: South

	1	2	3	4	5	6	7
1	.9980493		.0000001	.0000002	.0000025		.0019557
2		.9520000	.0080000		.0040000		.0120000
3			.9810997	.0017182		.0051546	.0120275
4				.9347826			.0652170
5			.0179856		.9559353	.0053957	.0206835
6		.3703704			.6296296		
7							1.0000000

Region 3: California

	1	2	3	4	5	6	7
1	.9979254		.0000001	.0000001	.0000039		.0020789
2		.9873737			.0101010		.0025253
3			.9884135		.0008913	.0026738	.0080214
4			.2142857	.7857143			
5			.0056582		.9769898	.0041493	.0132026
6		.8571429			.0714286		.0714286
7							1.0000000

Source: As in Table 3-4

Table -12
Homogeneous MLE
Markov Matrixes (Monthly Probabilities)
Region 1: Boston Megalopolis
4 Age Categories: No Sex Distinction

Age Group One
Age 0-14

Receiving States

Sending States	1	2	3	4	5	6	7
1	.9999719				.0000002		.0000279
2							
3							
4							
5					1.0000000		
6							
7							1.0000000

Age Group Two
Age 15-44

Receiving States

Sending States	1	2	3	4	5	6	7
1	.9998549				.0000029		.0001547
2		.9907407			.0061728		.0030864
3			.9914163			.0042918	.0042918
4							
5			.0025381		.9796954	.0152284	.0025381
6		1.0000000					
7							1.0000000

Age Group Three
Age 45-64

Receiving States

Sending States	1	2	3	4	5	6	7
1	.9988613				.0000067	.0000002	.0011318
2		.9784483			.0129310		.0086207
3			.9831224			.0168776	
4			.1000000	.9000000			
5			.0039474		.9723684	.0144737	.0092105
6		1.0000000					
7							1.0000000

Source: RTI National Dialysis Registry data
computed from raw data by Roy Littlejohn Associates

(CONTINUED)

Age Group Four
Age 65 +

	Receiving States						
	1	2	3	4	5	6	7
ing 1	.9917597				.0000058		.0082344
tes 2		1.0000000					
3							
4							
5					.9700000	.0100000	.0200000
6		1.0000000					
7							1.0000000

Source: RTI National Dialysis Registry data
computed from raw data by Roy Littlejohn Associates

Table 3-13
RTI Homogeneous Bayesian
Markov Matrixes (Monthly Probabilities)
Region 1: Boston Megalopolis
4 Age Categories: No Sex Distinction

Age 0-14

	1	2	3	4	5	6	7
1	.9999659		.0000012	.0000012	.0000014	.0000012	.0000290
2		.1715160	.1715160	.1715160	.1715160	.1715160	.1424200
3			.2143950	.2143950	.2143950	.2143950	.1424200
4			.2143950	.2143950	.2143950	.2143950	.1424200
5			.2091975	.2091975	.2334400	.2091975	.1389674
6		.1715160	.1715160	.1715160	.1715160	.1715160	.1424200
7							1.0000000

Age 15-44

	1	2	3	4	5	6	7
1	.9998516		.0000007	.0000007	.0000035	.0000007	.0001553
2		.9002156	.0189527	.0189527	.0244434	.0189527	.0184829
3			.8769603	.0315806	.0315806	.0352403	.0246383
4			.2143950	.2143950	.2143950	.2143950	.1424200
5			.0128336	.0104188	.9425046	.0249072	.0093358
6		.3617898	.1321248	.1321248	.1321248	.1321248	.1097111
7							1.0000000

Age 45-64

	1	2	3	4	5	6	7
1	.9988544		.0000014	.0000014	.0000081	.0000016	.0011330
2		.8591497	.0253573	.0253573	.0363766	.0253573	.0284019
3			.8715217	.0311250	.0311250	.0455524	.0206759
4			.1916298	.3508338	.1717293	.1717293	.1140777
5			.0145322	.0107834	.9342448	.0245291	.0159105
6		.4371902	.1165151	.1165151	.1165151	.1165151	.0967494
7							1.0000000

Age 65 +

	1	2	3	4	5	6	7
1	.9917477		.0000025	.0000025	.0000084	.0000025	.0082364
2		.4465314	.1145812	.1145812	.1145812	.1145812	.0951436
3			.2143950	.2143950	.2143950	.2143950	.1424200
4			.2143950	.2143950	.2143950	.2143950	.1424200
5			.0634756	.0634756	.7453737	.0705055	.0571699
6		.1916055	.1673580	.1673580	.1673580	.1673580	.1389674
7							1.0000000

Table 3-14

RTI Homogeneous MLE
Markov Matrixes (Monthly Probabilities)
Region 2 (South)
4 Age Categories

Age 0-14 (6 obs. in sample)

	1	2	3	4	5	6	7
1	.9999227				.0000001		.0000789
2		1.000000					
3			1.0000000				
4							
5			.0208333		.9375000	.0208333	.0208333
6		1.000000					
7							1.0000000

Age 15-44 (159 obs. in sample)

	1	2	3	4	5	6	7
1	.9998300		.0000001		.0000019		.0001700
2		.9729242	.0072202				.0108303
3			.9737188			.0131406	.0131406
4			.2500000	.2500000		.2500000	.2500000
5			.0252366	.0007886	.9447950	.0205047	.0086751
6		.9444444			.0555556		
7							1.0000000

Age 45-64 (121 obs. in sample)

	1	2	3	4	5	6	7
1	.9990862		.0000001	.0000002	.0000033		.0009173
2		.9794239	.0082305				.0123457
3			.9825175	.0017483		.0052448	.0104895
4				.9347826		.0058027	.0652174
5			.0193424		.9584139		.0164410
6		.9090909			.0909091		
7							1.0000000

Age 65 + (8 obs. in sample)

	1	2	3	4	5	6	7
1	.9956470				.0000007		.0043616
2							
3			.9000000				.1000000
4							
5					.9473684		.0526316
6					1.0000000		
7							1.0000000

Source: RTI National Dialysis Registry data
Computed from raw data by Roy Littlejohn Associates

Table 3-15

RTI Homogeneous Bayesian
Markov Matrixes (Monthly Probabilities)
Region 2: (South)
4 Age Categories

Age 0-14

	1	2	3	4	5	6	7
1	.9999215		.0000002	.0000002	.0000004	.0000002	.0000791
2		.4275282	.1185153	.1185153	.1185153	.1185153	.0984104
3			.3307809	.1826328	.1826328	.1826328	.1213207
4			.2143950	.2143950	.2143950	.2148950	.1424200
5			.1091150	.0977836	.6076986	.1091150	.0762879
6		.1916005	.1673580	.1673580	.1673580	.1673580	.1389674
7							1.0000000

Age 15-44

	1	2	3	4	5	6	7
1	.9998293		.0000002	.0000002	.0000021	.0000001	.0001701
2		.9186429	.0183484	.0116172	.0200312	.0116172	.0197432
3			.9355749	.0107699	.0107699	.0232504	.0196348
4			.2176135	.2176135	.1950147	.2176135	.1521447
5			.0310326	.0073549	.9216188	.0264498	.0127801
6		.5364396	.0905380	.0905380	.1167675	.0905380	.0751791
7							1.0000000

Age 45-64

	1	2	3	4	5	6	7
1	.9990846		.0000004	.0000006	.0000036	.0000003	.0009175
2		.8646197	.0314334	.0243725	.0243725	.0243725	.0308293
3			.9308265	.0160283	.0143932	.0192897	.0194576
4			.1000510	.5986017	.1000510	.1000510	.1012453
5			.0274537	.0089223	.9271526	.0144818	.0219898
6		.3298248	.1347028	.1347028	.1542150	.1347028	.1118518
7							1.0000000

Age 65 +

	1	2	3	4	5	6	7
1	.9956433		.0000008	.0000008	.0000014	.0000008	.0043622
2		.1461062	.1461062	.1461062	.1672702	.1461062	.1213207
3			.3508338	.1717293	.1717293	.1717293	.1339782
4			.2143950	.2143950	.2143950	.2143950	.1424200
5			.0742314	.0742314	.6935862	.0742314	.0837196
6		.1227292	.1227292	.1227292	.4071737	.1227292	.1019094
7							1.0000000

Table 5-16

RTI Homogeneous MLE
Markov Matrixes (Monthly Probabilities)
Region 3 (California)
4 Age Categories

Age 0-14 (10 obs. in sample)

	1	2	3	4	5	6	7
1	.9999683				.0000001		.0000339
2		.9914530			.0085470		
3							
4							
5					.8936170	.0851064	.0212766
6		1.0000000					
7							1.0000000

Age 15-44 (172 obs. in sample)

	1	2	3	4	5	6	7
1	.9998602				.0000015		.0001408
2		.9888535			.0087580		.0023885
3			.9767055			.0133111	.0099834
4							
5			.0085373		.9607285	.0216278	.0091064
6					.1304348		
7							1.0000000

Age 45-64 (203 obs. in sample)

	1	2	3	4	5	6	7
1	.9991408		.0000001	.0000001	.0000044		.0008633
2		.9866310			.0106952		.0026738
3			.9880624		.0009183	.0027548	.0082645
4			.2142857	.7857143			
5			.0055479		.9768840	.0050855	.0124827
6		.8461538			.0769231		.0769231
7							1.0000000

Age 65 + (35 obs. in sample)

	1	2	3	4	5	6	7
1	.9951154				.0000026		.0048897
2		1.0000000					
3			1.0000000				
4							
5			.0061475		.9774590		.0163734
6		1.0000000					
7							1.0000000

Source: RTI National Dialysis Registry data
Computed from raw data
By Roy Littlejohn Associates

Table 3-17

RTI Homogeneous Bayesian
Markov Matrixes (Monthly Probabilities)
Region 3 (California)
4 Age Categories

Age 0-14

	1	2	3	4	5	6	7
1	.9999671		.0000002	.0000002	.0000004	.0000002	.0000341
2		.7815804	.0439016	.0439016	.0502609	.0439016	.0364541
3			.2143950	.2143950	.2143950	.2143950	.1424200
4			.2143950	.2143950	.2143950	.2143950	.1424200
5			.0989043	.0989043	.5802796	.1447496	.0771622
6		.2464072	.1560117	.1560117	.1560117	.1560117	.1295459
7							1.0000000

Age 15-44

	1	2	3	4	5	6	7
1	.9998596		.0000002	.0000001	.0000017	.0000001	.0001409
2		.9634743	.0053258	.0053258	.0138118	.0053258	.0067367
3			.9288568	.0134572	.0134572	.0259328	.0182961
4			.2143950	.2143950	.2143950	.2143950	.1424200
5			.0131402	.0047988	.9434892	.0259304	.0120853
6		.5438089	.0800408	.0800408	.1496060	.0800408	.0664627
7							1.0000000

Age 45-64

	1	2	3	4	5	6	7
1	.9991394		.0000004	.0000004	.0000047	.0000003	.0008636
2		.9074315	.0166651	.0166651	.0263211	.0166651	.0162520
3			.9604865	.0076417	.0085273	.0102983	.0130462
4			.2143668	.3618322	.1590673	.1590673	.1056664
5			.0093589	.0039149	.9625176	.0089053	.0148497
6		.3362163	.1296436	.1296436	.1484229	.1296436	.1264301
7							1.0000000

Age 65 +

	1	2	3	4	5	6	7
1	.9951122		.0000007	.0000007	.0000033	.0000007	.0048902
2		.4643136	.1108999	.1108999	.1108999	.1108999	.0920868
3			.5683194	.1178075	.1178075	.1178075	.0782581
4			.2143950	.2143950	.2143950	.2143950	.1424200
5			.0219734	.0163050	.9175803	.0163050	.0259469
6		.1916005	.1673580	.1673580	.1673580	.1673580	.1389674
7							1.0000000

Table 3-18

Chi Square Statistics Tests
of the Effect of Age on Parameter
Estimates: Pooled (1 + 2, 3 + 4) Contrasted
with Unpooled (1, 2, 3, 4)

	2	3	4	5	6
Region I (Boston Megalopolis)					
Ages:					
0-14	-	-	-	.204	-
15-44	101.140	96.140	-	74.724	70.118
45-64	89.477	87.413	43.665	61.429	78.007
65 +	9.646*	-	-	12.536	4.106*
	2	3	4	5	6
Region 2 (South)					
Ages:					
0-14	4.675*	1.328*	-	2.287*	2.827*
15-44	82.816	82.997	25.092	42.520	78.789
45-64	108.192	87.901	92.262	55.181	89.275
65 +	39.757	2.066*	-	14.791	100.709
	2	3	4	5	6
Region 3 (California)					
Ages:					
0-14	7.926*	-	-	27.357	10.566*
15-44	84.209	85.363	-	54.254	67.509
45-64	91.187	87.184	40.177	45.363	60.005
65 +	6.992*	3.530*	-	22.693	6.055*

* Homogeneous at .95 level.

Source: RTI National Dialysis
Computed from raw data
by Roy Littlejohn Associates, Inc.

Table 3-19

Representative Chi Square Statistics: California Females Age Group 45-64

N=82

State	Degrees of Freedom	Chi-Square Statistics	$C^2 = \frac{X^2}{d.f.}$	Confidence Level	Homogeneous
2	120	21.99	.183	Greater than .9995	(Yes)
3	96	45.81	.477	Greater than .9995	(Yes)
4	96	5.00	.052	Greater than .9995	(Yes)
5	96	85.59	.892	Greater than .7000	(?)
6	120	10.00	.083	Greater than .9995	(Yes)

Degrees of freedom = (S-1) X (T-1)

S = 1....7 (States)
T = 1...24 (Time Periods)

Actual degrees of freedom used represented adjustment for parameters that were assumed structurally equal to zero.

Source: RTI National Dialysis Registry data
Computed from raw data by Roy Littlejohn Associates

Table 20

Chi Square Statistics: Simultaneous Confidence Tests of the Homogeneity of Parameter Estimates: Each State By Region and Age

		1	2	3	4	5	6	Combined States 7
Region 1								
Ages:								
0-14	MLE	88.03*	-	-	-	-	-	88.03*
	Bayes	11.14*	-	-	-	4.68*		15.82*
15-44	MLE	96.66*	149.29*	170.63	-	236.58	-	653.16*
	Bayes	78.08*	30.54*	22.02*	-	81.17*	31.22*	243.03*
45-64	MLE	196.28	274.94	73.58*	40.00*	205.08	-	789.88*
	Bayes	100.91*	104.06*	24.08*	24.53*	91.71	34.62	379.91*
65 +	MLE	410.92	-	-	-	157.38*	-	568.30*
	Bayes	371.11	42.76*	-	-	75.17*	6.02*	495.06*
Region 2								
Ages:								
0-14	MLE	76.02*	-	-	-	199.82	-	275.84*
	Bayes	27.90*	11.03*	16.82*	-	35.28*	6.02*	97.05*
15-44	MLE	249.44	285.32	126.31*	132.00*	306.86	55.06*	1154.99
	Bayes	118.80*	127.71*	77.42*	28.52*	180.28*	36.93*	569.66*
45-64	MLE	215.05	224.66	303.31	49.49*	260.05	19.80*	1072.36
	Bayes	103.31*	78.01*	101.35*	47.01*	169.27	24.77*	523.72*
65 +	MLE	233.17	-	40.00*	-	48.63*	-	321.80*
	Bayes	180.19	13.35*	27.70*	-	24.51*	14.41*	260.16*
Region 3								
Ages:								
0-14	MLE	76.00*	90.37*	-	-	159.65*	-	326.02*
	Bayes	27.88*	15.65	-	-	38.88*	16.16*	98.57*
15-44	MLE	168.80	126.28*	172.28	-	260.92	45.87*	774.15*
	Bayes	97.08*	57.59*	85.23*	-	194.06	36.55*	470.51*
45-64	MLE	351.96	166.78	370.29	44.12*	353.29	66.18*	1352.62
	Bayes	139.26*	42.75*	132.86*	31.82*	237.24*	48.31*	632.24*
65 +	MLE	283.25	-	-	-	142.73*	-	425.98*
	Bayes	268.52	2.48*	16.81*	-	63.50*	6.02*	357.33*

* Homogeneous at .95 level.

Table 3-21

Relative MLE Parameter Estimates

Pooled Age Groups $\left(\frac{P^{(1+2)}}{P^{(1+2)} + P^{(3+4)}}\right)$ By Region

Region 1

	1	2	3	4	5	6	7
1	.501	–	–	–	.229	.000	.029
2	–	.503	–	–	.341		.280
3	–	–	.502	–	–	.203	1.000
4	–	–	.000	.000	–	–	–
5	–	–	.421	–	.503	.522	.195
6	–	.500	–	–	–	–	–
7	–	–	–	–	–	–	–

Region 2

	1	2	3	4	5	6	7
1	.500	–	.500	.000	.342	–	.065
2	–	.506	.466		.686	–	.466
3	–	–	.499	.000	–	.717	.520
4	–	–	1.000	.211	–	1.000	.793
5	–	–	.583	1.000	.497	.792	.326
6	–	.719	–	–	–	.079	
7	–	–	–	–	–	–	–

Region 3

	1	2	3	4	5	6	7
1	.500		.000	.000	.204	–	.047
2	–	.500	–	–	.464	–	.464
3	–	–	.497	–	.000	.833	.554
4	–	–	.000	.000	–	–	–
5	–	–	.595	–	.495	.849	.417
6	–	.507	–	–	.627	–	.000
7	–	–	–	–	–	–	–

Table 3-22

Incidence of Chronic Kidney Disease
Implied by Model Data
Patients/Million, by Age, Region
1972 and 1973

	1972	1973
Overall Incidence (Pooled Age, Region)	23.5	21.9
Region 1: Boston Megalopolis Age 0-44	19.0	24.7
Region 1: Boston Megalopolis Age 45 +	58.6	82.0
Region 2: South Age 0-44	15.0	15.6
Region 2: South Age 45 +	27.6	33.0
Region 3: California Age 0-44	12.8	11.6
Region 3: California Age 45 +	45.9	44.1

Sources:

Population data estimates: See Table 1-1

Chronic patients: RTI National Dialysis Registry
Estimated by Roy Littejohn Associates, Inc.

CHAPTER FOUR

The Steady State Matrix As a Planning Tool

It is possible to compare the regional differences in disease treatment systems by computing limiting state and state occupancy statistics of the Markov model. These computations will not change the previous substantive analysis, but will provide additional perspective to the analysis. They will also prove useful later in estimating treatment costs. A brief technical discussion of computation techniques appears in Appendix F.

A. Steady State Probabilities

As this Markov process operates over time, so long as inputs into and outputs from the system are either stabilized or eliminated, the distribution of patients will attain a kind of stability in which one's position in the system bears no relation to one's state on entry. This limiting distribution is the steady state distribution.

When a Markov system contains one or more absorbing states (such as death in the RLA model), the steady state approached will have all system members absorbed and none left in the transient states. For this reason, it is plausible to delete the absorbing state and examine the steady state characteristics of "survivors." Thus it is also true that such a solution sacrifices realism to achieve a quasi-stability in state distributions. The reader should also remember that it will normally be impossible to observe steady states of a system from raw sample data. The distribution of

patients across disease treatment states at any given time is a function not only of the underlying structural characteristics that produce a survivor steady state, but also of the rate of system input (birth, population aging) and output (death).

The steady state results for the three regions of RLA's model appear in Table 4-1. Using Region 1, these data can be interpreted in the following way: were one permitted to observe the process of patient flows among the transient (that is, disease-treatment) states of the system over time, one would see that this interchange tends toward a distribution in which 56% of the population remains stable following a transplant, 8% are on home dialysis, 35% are on institutional hemodialysis and 1% are receiving a transplant in any given month. State 4, peritoneal dialysis, acts only as a short run conduit to other states, and has no long run occupancy.

Comments made above about regional differences in treatment systems are reinforced in steady state analysis. Once again, one notes the discrepancy between the South and the other two regions in use of home dialysis: 53% of Southern patients remain on home dialysis in the long run, compared to 16% in California and only 8% in the Boston megalopolis. In contrast, more patients in Boston (56%) and California (50%) remain stable following transplant than is true for the South (32%). This results less from a higher transplant rate (the long-term rate of transplant differs insignificantly among the regions) than from a higher survival of grafts.

Finally, institutional hemodialysis constitutes the dialysis treatment of choice in the Boston megalopolis (35%) and in California (33%), but not in the South (13%). It should be noted that a weak tendency toward use of maintenance peritoneal dialysis appears in the Southern data (a limiting-state probability of 1%), but not in data for the other regions. It is likely that data should show some such activity for all three regions, but since no patient flows from other states into peritoneal dialysis were observed, maximum likelihood estimates produce a long run probability of zero for peritoneal dialysis.

In summary, though the notion of a steady state abstracts somewhat from the realistic and observable behavior of a complex system, computation of steady state probabilities gives one a look at the long-run target of such a system. The solution for regional matrixes of the RLA model confirms the earlier observation that the Southern region relies relatively heavily on home dialysis, and will therefore tend to a distribution in which most patients follow this treatment. Boston and California retain relatively higher percentages of patients in post-transplant stability and on institutional hemodialysis.

B. Holding and First Passage Times

Markov probabilities project the numbers of patients that move from state-to-state in a time period. It is often instructive to ask a related question: how long does it take for patients to make various moves among states? Since the dimension of the basic probabilities is patients/time period, it is not surprising that the answer to a question about time periods/patient uses the probabilities in inverse form.

The average time that a patient who has entered state i stays in that state before leaving is known as the mean holding time for state i. Mean holding times for the three regions are presented in Table 4-1. Notice that these computations include State 7 (death), and are thus based on the original probabilities in states 2 - 7 of the matrixes (in contrast to the "survivor" probabilities used in calculating steady states).

Clearly the mean holding times for all states except peritoneal dialysis and greater in Boston and California than they are in the South. Holding in state 2, post-transplant stable for regions 1 and 3 averages almost twice as long as in the South; 72 months and 88 months, respectively, compared to 39 months. Holding on home dialysis is longer for Boston patients on home (94 months) and peritoneal dialysis (10 months); the comparative figures for the South are 44 months and 8 months, and for California, 64 months and 3 months. Holding times are identical for transplant in the three regions, because no observation of consecutive transplants appeared in the RLA sample. Thus, the holding time is one month by definition (see Appendix F).

The sum of holding times yields total time spent by the average system member in the system's transient states. For the present analysis, one might interpret this figure as total time on treatment until death. Again, the result confirms the analysis done earlier: life expectancy for a kidney patient in the South is less than life expectancy in Boston and California. In fact, total holding time in Boston (220 months or about 18 years) is nearly double

the Southern time (112 months or about 9 years) and comparable to California (193 months or about 16 years). These times, it should be remembered, are crude survivor statistics, unadjusted for the relevant demographic factors. It is doubtful that age-adjustment would change the results, however, since the Southern population was shown to be younger than the populations in the Boston megalopolis and in California.

First passage times (see Table 4-1) show how many time periods are required before the average patient leaves state i and goes to state j. If i = j, the result describes the number of time periods required to return to the original state, once the patient has left, and is called the mean recurrence time. Mean recurrence times are presented on the diagonal (states 2 - 6) of the matrixes in Table 4-1.

Mean recurrence times are the reciprocal of the steady state probabilities, and thus add no new information.[1] Obviously, states which tend to collect most patients in the long run, such as state 2 in California and Boston, have a high mean recurrence (2 months for both). On the other hand, once transplanted, a repeat transplant comes, on average, 170 months later in Boston, 146 months in the South, and 195 months in California.[2]

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[1] See Appendix F for technical discussion.

[2] Regional differences come from the fact that mean recurrence times were computed using steady state probabilities that were accurate to four decimal places. Differences do not appear in Table 4-1, where results are rounded to two decimals.

Table 4-1

State Occupancy Statistics, by Region (Pooled Age Groups)
Steady State Probabilities, Mean Recurrence and First Passage Times;
Mean Holding Times

Region 1 Boston Megalopolis		Mean Recurrence & First Passage Times						Mean Holding Times (months)	Steady State Probabilities
		2	3	4	5	6	7		
Stable	2	1.78	72.39	72.39	72.00	72.38	72.39	72.00	$P_2 = .56$
Home Dialysis	3	93.87	13.11	94.38	94.32	93.80	94.38	93.80	$P_3 = .08$
Peritoneal Dialysis	4	19.39	10.00	-	19.43	19.38	19.44	10.00	$P_4 = 0$
Institutional Hemodialysis	5	43.77	44.34	44.51	2.81	43.51	44.51	43.34	$P_5 = .35$
Transplant	6	8.11	68.38	68.41	60.85	170.45	68.41	1.00	$P_6 = .01$
								$\Sigma =$ 220.2 (18 yrs.)	$\Sigma = 1.00$
Region 2 Rural South	2	3.09	39.01	39.34	39.18	39.34	39.20	38.86	$P_2 = .32$
	3	43.64	1.89	43.89	43.83	43.55	43.88	43.55	$P_3 = .53$
	4	9.35	8.45	96.46	8.02	9.20	9.91	8.33	$P_4 = .01$
	5	21.27	20.31	20.86	7.63	21.17	21.66	20.22	$P_5 = .13$
	6	7.31	34.46	34.85	28.55	145.98	35.05	1.00	$P_6 = .01$
								$\Sigma =$ 111.96 (9 yrs.)	$\Sigma = 1.00$
Region 3 California	2	1.99	88.79	88.79	88.45	88.78	88.79	88.45	$P_2 = .50$
	3	63.87	6.21	64.31	64.31	63.83	64.36	63.81	$P_3 = .16$
	4	26.87	2.64	-	27.03	26.85	27.05	2.64	$P_4 = 0$
	5	37.28	37.99	38.10	3.02	37.22	38.20	37.00	$P_5 = .33$
	6	5.08	83.06	74.13	78.39	194.98	82.88	1.00	$P_6 = .01$
								$\Sigma =$ 192.90 (16 yrs.)	$\Sigma = 1.00$

First passage times, for the most part, fluctuate about the mean holding times, as discussed in Appendix F. Exceptions are passage from state 4 in Regions 1 and 3 and passage from state 6 in all three regions. State 4, peritoneal dialysis, was discussed above - the passage time pattern observed reflects the fact that state 4 inhabitants exit rather quickly to home dialysis and then have no direct access back into the peritoneal state. Transplants show relatively fast transition to stable (8 months for Boston, 7 months for the South and 5 months for California); since with $P_{66} = 0$, there is no computable mean recurrence time, the P_{62} transition, in a sense, describes the "retention" of a transplant patient in a successful operation. Transitions from transplant to other types of dialysis and to death are similar within regions.

To summarize, state occupancy statistics describe the time in and among states for an average patient. Since they are computed from one-step homogeneous probabilities and from steady state probabilities, they reflect the structural characteristics of the model described earlier.

Chapter Five

Costs of Kidney Treatment Activities

Empirical kidney treatment cost data can be used to guide policy decisions on which treatment modes should be encouraged by explicit administrative or legislative fiat or, more subtly, by the allocation of public expenditures. Ideally, one might hope to identify, through specification of a structural model, those forces that not only set average levels of treatment cost but that also lead to cost variations under different assumptions about producer size, product quality and the like. In the absence of such a structural model, most researchers have used average costs, with some measure of variation about the average, to make recommendations about treatment strategies.[1] RLA contends, however, that information contained in the input/output system described above adds depth to cost comparisons that is lacking in straight comparisons of averages.

For example, because average yearly costs of institutional hemodialysis exceed the yearly costs of home dialysis, it has been argued that all dialysis patients that are physically and psychologically qualified should be placed in training for home dialysis.[2]

To back this claim, the researcher should be able to discuss the structure of the system from which the empirical cost figures were computed. Institutional dialysis charges derive from patients dialyzed temporarily, prior to transplant, from those dialyzed between transplants or subsequent to transplant failure, from patients in training for home programs and from patients for whom institutional dialysis is the treatment of choice. Some of the variation

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[1]See the recently published study of kidney treatment costs by the General Accounting Office (REF 283)

[2]Ibid.

in cost averages may derive from this mix, but more basically, an individual started in home or institutional dialysis may or may not remain in the initial state. The expected cost of dialysis, based on movement among treatment modes, better describes the cost actually incurred.

Thus, if one patient begins in institutional dialysis and another begins in home dialysis, at a point in time, subsequent charges will reflect not only the average costs of institutional and home dialysis but also the probabilities of moving to various other treatment modes or to death. The RLA model makes possible such analysis by computing average times spent by patients remaining in or moving among various states. And in a limiting or long-range sense, there tends to be an underlying stability in the distribution of patients among states that suggests where the system is moving. Long-run total costs of treatment can be guessed, based on this "steady state" distribution of the patient population.

A. RLA Cost Estimates

RLA received tapes summarizing Medicare charge data on kidney patients received by the Social Security Administration. SSA reimburses kidney patients for treatment expenses, and patient monthly charge forms, SSA-2743, constitute an important set of cost data on kidney disease. The tapes contained observations on 3,016 patients, covered from February 28, 1973 to February 28, 1975. The observation units, however, are patient records, of which 29,246 appeared on the tapes. RLA drew a 25% random sample of observations

totaling 7,296 records, of which 17% came from Region 1, 21% from Region 2 and 62% from Region 3. Computations on average costs were broken down by region and age, to correspond with the classification system in RLA's stochastic model. The averages, by state number, are:

State 3: Average monthly home dialysis charges: monthly rental or purchase charges for equipment, plus monthly supply charges.

State 4: No cost data available for peritoneal dialysis.

State 5: Average dialysis charge per month for institutional dialysis assuming eight treatments per month. This average submerges the possibility of multiple settings over a period of institutional dialysis (a setting defined as in-patient hospital, out-patient hospital, limited care facility, self dialysis unit and training dialysis).

State 6: Transplant costs were derived from GAO figures, since the SSA files do not show total transplant charges including physician fees.

Tables 5-1 and 5-2 present regional average cost figures for home and institutional hemodialysis. To make comparable the institutional and home dialysis charges, institutional per dialysis costs have been converted to monthly values, with an estimate of eight sessions per month. Results are given in Table 5-3.

Tests using one-way analysis of variance force rejection of the hypothesis that no regional difference exists in average cost for

Table 5-1 Average Monthly
Home Dialysis Charges, February 1973 - February 1975

Region I	Average Charge (dollars)	Standard Error (dollars)	Sample Size
Massachusetts Rhode Island	148.18	185.96	120
Region II			
Mississippi North Carolina South Carolina Tennessee Virginia	301.28	355.26	169
Region III			
California	288.01	376.63	416

Source: Computed by Roy Littlejohn Associates from data tapes supplied by the Social Security Administration.

Table 5-2 Average Charge per Treatment, Institutional Hemodialysis, by Region, February, 1973 - February, 1975

Region I	Average Charge (dollars)	Standard Error (dollars)	Sample Size
Massachusetts Rhode Island	149.88	24.79	894
Region II			
Mississippi North Carolina South Carolina Tennessee Virginia	147.19	24.89	1013
Region III			
California	187.24	39.35	3374

Source: Computed by Roy Littlejohn Associates from data tapes supplied by the Social Security Administration.

Table 5-3 Average Institutional Dialysis Charge Per Treatment by Age and Region February, 1973 - February, 1975

Age	Region I Massachusetts Rhode Island Average charge (dollars)	Sample Size	Region II Miss., N.C. S.C., Tenn. and Virginia Average charge (dollars)	Sample Size	Region III California Average charge (dollars)	Sample Size
0-44	150.19	290	147.90	461	182.92	952
0-19	158.62	21	132.17	35	173.88	84
20-29	148.27	117	149.55	144	182.97	219
30-34	151.16	45	152.30	90	184.50	194
35-39	150.07	43	146.88	79	190.33	172
40-44	150.33	64	147.87	113	179.99	283
45+	149.73	604	146.62	555	188.94	2422
45-49	144.21	73	148.39	145	182.62	370
50-54	154.37	85	149.19	113	190.37	406
55-59	150.26	107	145.29	123	188.20	426
60-64	145.84	135	143.91	99	186.14	448
65+	152.07	204	145.05	75	193.26	772

Source: Computed by Roy Littlejohn Associates from data tapes supplied by the Social Security Administration.

either treatment mode. It is interesting to note that no clear pattern in regional ranking emerges: the South's average home dialysis charge is highest of the three, whereas California's institutional dialysis charge is highest in its category. Further the data suggest a homogeneity of charges for institutional dialysis that is absent in the home dialysis figures.[1]

If one compares home and institutional dialysis within regions, there are clear through inexplicable differences to note. Institutional dialysis is 8.1 times as expensive as home dialysis in Region 1, compared to 3.9 and 5.2 times in Region 2 and 3 respectively. The RLA model shows that home dialysis constitutes a treatment mode that is preferred and much used in the South but little used in the Boston area. An economist would argue that these regional relative costs and treatment pattern suggest scale diseconomies, but in the absence of further institutional detail it would be difficult to test his hypothesis from these data.

Age-specific tests show a greater contrast in home dialysis charges than institutional charges between the "old" (45^+) and "young" (0-44) patients (see Table 5-4). One should suppress the urge to attribute these discrepancies to age alone.Slicing the data into finer age categories shows a ragged pattern of age-specific

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[1]The institutional dialysis averages are 5 to 6 times the size of their standard deviations. The extent of variation across regions is large for home dialysis, compared to institutional dialysis. If one compares the range between the highest and lowest averages (40.05 for per treatment institutional dialysis, 153.10 for home) measured relative to the three region average (173.23 for institutional, 267.39 for home dialysis) the difference is striking; .23 for institutional dialysis and .57 for home dialysis.

Table 5-4 Average One Month Treatment Charge, Selected Kidney Treatment Modalities, by region.

	Region I Boston Megalopolis	Region II Southern Rural	Region III California
Home Dialysis	148* (186)[1] n=120	301* (355)[1] n=169	288* (377)[1] n=416
Institutional Hemodialysis	1199* (198) n=892	1177* (199) n=1013	1498* (315) n=3374
Transplant	12,800[2]	12,800[2]	12,800[2]
Ratio of institutional charge to home dialysis charge	8.1	3.9	5.2

Source: Medicare records of Social Security Administration

1 Standard errors given in parentheses
2 Data from Social Security Administration were supplemented by GAO figures (REF 283) latter were undifferentiated regionally.
* Significantly different at .99 level

charges, for both home and institutional dialysis. Moreover, any simplistic hypothesis that relates age to cost seems weak in the face of these results; in Region 1, costs drop with age for both treatment modes: in Region 2, costs rise for home dialysis and remain virtually unchanged for institutional dialysis; in Region 3, institutional dialysis costs rise with age, as do home dialysis costs.

In summary, the data from RLA's analysis of the SSA records show no clear patterns of age or regional impact on cost averages. Institutional costs per month clearly exceed home dialysis costs per month, and the discrepancy varies across regions. What the data do suggest is that many aspects of regional treatment systems, demographic factors and the like need to be probed before valid tests of cost hypothesis are possible.

B. Model Cost Estimates

The detailed cost data discussed above are meant to show the relationship between age and regional cost averages. In order to estimate the costs implied by the RLA model, SSA estimates were combined to produce monthly averages. These figures, with standard errors in parenthesis, are presented in Table 5-4. Note that the transplant cost estimate comes from the GAO report (REF 283); the standard error for this figure was unavailable. RLA was unable to collect data for the costs of peritoneal dialysis. In the subsequent estimates, this state is ignored. Patients with functioning transplants (state 2) were assumed to incur no costs, and are so

treated in the following discussion. By leaving out costs of peritoneal dialysis and any incidental costs incurred by patients in the stable state, RLA has clearly underestimated total costs of kidney treatment.

Table 5-5 shows expected costs per patient by region computed two ways. Expected long-run monthly costs per patient are computed by combining regional cost data for home and institutional dialysis, and the transplant cost estimate, with long-run (steady-state) percentages in these three states by region (normalized to sum to 1.0). The result is a set of averages that weights each treatment cost by the probability it will be used and then sums to the over-all average. Column (1) shows the South, which depends on home dialysis, can expect a lower monthly cost per patient ($717) than Boston ($1,242) or California ($1,337). It must be remembered, of course, that these expectations merely project current practice in the regions. This model cannot assess the impact of changed treatment mix, since the impact of such changes on average costs cannot be specified.

From another point of view, regional costs differ when computed over the patient's expected life time in the kidney treatment system. Column (2) of table 5-5 shows the total costs spent for each of the three treatment modes, by region. The sum of these is the total cost of care per patient. Each component was computed by multiplying the cost/month, by treatment and region, times the mean holding

Table 5-5 Cost Estimates, based on RLA Model:
Expected Monthly and Total Cost/Patient

	Expected Long Run Costs Per Month Per Patient (1)	Expected Costs Per Patient From Entry Until Death (2)			
		Home Dialysis	Institutional D.	Transplant	Total
Region I	$ 1,241.84	$ 13,882	$ 51,965	$ 12,800	$78,647
Region II	$ 717.42	$ 13,109	$ 23,799	$ 12,800	$49,708
Region III	$ 1,336.84	$ 18,377	$ 55,426	$ 12,800	$86,603

time (in months), by treatment and region. Once again, the Southern patient's cost falls far below costs incurred by patients in Boston and California: almost $50,000, compared to $79,000 for Boston and $87,000 for California. It is important to remember in interpreting these data that the South's advantage depends not only on a relatively heavy dependence on home dialysis but also on a relatively shorter life expectancy.

These figures suggest that a transplant pays, even in the South, if done immediately upon entry and if wholly successful. However, once stable, a transplant patient on average can expect institutional dialysis in 72 months (Boston), 39 months (the South) or 88 months (California). If the patient remains on institutional dialysis until death, he can expect 45 months at a total cost of $53,995 for Boston (making the transplant + dialysis cost = $66,755), 22 months at a total cost of $25,894 for the South (making the transplant + dialysis cost = $38,694) and 38 months at a total cost of $56,924 for California (making the transplant + dialysis cost = $69,724). This is but an example. Numerous other treatment combinations are possible.

C. Scale Effects in Kidney Treatment

The cost forecasting approach described above implicitly assumes that expanding or contracting the size of the treatment facility will have no impact on the average level of operating costs. This assumption simplifies the forecasting process, but may do violence to reality. Since the government has effectively removed most financial restraints on patient effective demand for high-cost kidney treatment by promising full reimbursement, it is important to test the

effect of changes in volume on the unit costs of operation.

In a sense, two scale questions might be asked. One deals with the short run effects of a major jump in demand, and would be germane to the policy issue posed by the Social Security Kidney Amendment: what are the effects on average costs for the entire kidney treatment industry, regardless of the size of individual providers, if the demand for treatment changes markedly? Unfortunately, data do not permit a test of this type. A more limited test, using cross section data, asks: what are the likely effects of provider capacity expansion on average cost, assuming demand warrants such expansion? Put another way, are there gains (or losses) from trying to be bigger?

RLA's test of this question involved constructing a statistical test of the hypothesis that the average cost of per treatment of producing "X" treatments over a given time period depends on the size of the facility and the average cost of operating the facility at a level sufficient to produce the "X" treatments. Nursing costs were taken to be the most significant component of operating costs.

This test rejects the assumption that some unique minimum unit cost exists, to which all firms are pushed by competitive forces, which produces an industry populated by providers of equal size. Instead the behavior of cost over a range of sizes (represented by number of dialysis stations) is examined and the results used to test the hypothesis of scale economies. The relation takes on the fuctional form:

Average cost/dialysis = f (number of dialysis stations, average nursing cost per treatment)

1. Data

The data used in this test consist of thirteen cross-section observations on thirteen institutions that provided hemodialysis services in the state of California. The observation period is the month of November 1973. These data were collected by Peat, Marwick, Mitchell and Company for the California Regional Kidney Disease Program. The purpose of the data collection was to test the Regional Medical Program's "California Cost Reporting/Data Collection System" (CR/DC). The (CR/DC) system was also designed by Peat, Marwick, Mitchell and Company. All data definitions used in this study are taken from

The basic limitation of the data is that:

> The procedure used to draw a meaningful sample was limited by the volunteer nature of the study; however, a proper distribution of facility types by institutional setting and program diversity was achieved.

The data include observations on university hospital, profit, non-profit, and public facilities. The number of observations prevents separate analysis of these different facilities. It is the authors' opinion that because of the extreme care with which the data were apparently collected, the uniformity of definitions and research techniques, the careful attempt to insure a representative if not random sample, and the availability of small sample statistical techniques, these data are of relatively high quality and more than

adequate for econometric technique.

2. Tests

Functions based on the general relationship described above were fitted by least squares to the data. One set of equations dropped the nursing cost variable (set 1) and another included it (set 2).[1]

It is interesting to note that "optimum size" or lowest cost facility of 10 dialysis beds, ignoring variations in nursing costs, is associated with an average dialysis cost of $158.38. The cost associated with the optimum size including nursing cost variations (again, 10 stations) is $167.15. The actual average cost observed for the California CR/DC data was $184.69.

RLA estimated from the 25% sample of Social Security records that institutional dialysis costs average $187.24/treatment in California. The average reported by the GAO study for Los Angeles County seems quite puzzling in light of these results. GAO lists the average for hospitals as $259 per dialysis, with a range of $150 to $315, and $230 for non-hospital centers, with a range of $120 to $300. GAO further reports HEW information that center dialysis now averages about $160 per treatment (p.41), under the new government reimbursement scheme. This figure more nearly squares with

[1] Of the equations used in set 1, a quadratic form appeared to best represent the inter-relationship between cost and size. Since a cost relation showing normal scale economies and diseconomies has a "U" shape, this result bolsters the scale hypothesis. A quadratic form in set 2, with nursing cost added in, also dominates its group, further strengthening confidence in the hypothesis. For a complete technical discussion, see A. Headen, Scale Effects and Price Relations in the Provision of Chronic Hemodialysis Washington: Roy Littlejohn Associates, April 1975.

the California CR/DC and RLA results and, if true, appears barely to cover RLA's computed least-cost figure.

In summary, by fitting a function relating average cost/dialysis to facility size and nursing cost, RLA found support for the hypothesis that scale affects average cost over the range of observations. Thus forecasting using an assumption of constant cost is subject to error. Moreover, RLA's estimated minimum unit cost level appears to match well with HEW's impression of the average per dialysis charges under the new government reimbursement scheme.

CHAPTER SIX

VI. CONTRAST OF RLA MODEL WITH OTHER MODELS

It is possible, in principle, to compare this model to other models both as a statement about the structure of the kidney disease treatment system and as a usable forecasting tool. Other attempts to model formally the disease-treatment system have made use of the Markov process. Farrow, et al. (REF 108-110) produced a pioneering study of a London treatment facility. Another center-based study, by Blagg and Cooper (REF 92) uses the Markov formulation but predictions are applied to a regional catchment area. Growth is assumed; it is not built into the model as does the RLA version. Cost of model operation must be considered cheaper than the RLA model.

Plishkin (REF 339) and Parker and Nakamura (REF 335) have applied Markov techniques in models designed principally to simulate decision and control strategies for renal system planners. Plishkin's delineation of states differs from RLA's and his Markov matrix itself constitutes only part of a larger effort to model the system's dynamics in several difference equations. His estimates of parameters are drawn from the literature and informed opinion, and are thus useful for simulation only.

Parker and Nakamura (REF 335) designed a linear model to study the implications of cost and life expectancy optimizing strategies on the choice of treatment modes. They discuss the problem of modifying transition probabilities by deliberate policy. Once again, the numbers used to simulate the working of this model come from the literature and are not statistically testable.

Table 6-1

Region 3

Comparison of RLA Matrix and Cooper Matrix

Receiving States

			2	3	4	5	6	7
Sending States	2	RLA	.988	-	-	.009	-	.003
		C	.988	.001	.001	.003	*	.012
	3	RLA		.983	-	.001	.006	.010
		C		.980	.001		.009	.010
	4	RLA		.214	.786	-	-	-
		C		-	.882	.001	.001	.096
	5	RLA		.007		.969	.011	.012
		C		.208	.011	.692	.053	.036
	6	RLA	.843			.137		.020
		C	.981	.001	.001	.003	.001**	.013
	7	RLA						1.00
		C						1.00

*Impossible to estimate
**Residual .

Conversion:

RTI State	Cooper State (Ref 92)
2 Stable	6, 7 Living related and Cadaveric donor transplant
3 Home hemodialysis	5 Same
4 Peritoneal dialysis	3 Same
5 Institutional dialysis	2, 4 Center hemodialysis, hemodialys home training
6 Transplant	6, 7
7 Death	11

Sources: Northwest Kidney Center Study, completed by Cooper, and RLA matrix (pooled data)

Farrow's system states, though estimated from patient records, adhere to a rather strict process of channeling patients though six or so months of pre-transplant or pre-home dialysis training maintenance dialysis. Thus the components of this system depend crucially on the practice of this particular treatment center.

Blagg and Cooper base their approach on the Farrow paper, in a study of the Northwest Kidney Center in the state of Washington. Their states, which are less dependent on a rigid time pattern of treatments than are Farrow's, more resemble the states in the RLA study, and thus their summary matrix has been compared with the RLA matrix in Table 6-1. State one has been ignored in this comparison. In general, their values correspond closely with RLA's own results.

The most important distinction between the RLA and Blagg/Cooper matrixes comes in the nature of state 4 (peritoneal dialysis.) Apparently, the NWKC has experimented with home peritoneal dialysis, and generally relies on peritoneal dialysis more heavily than do many centers. NWKC appears to send more patients per month from institutional to home dialysis than do the centers in the RLA analysis (20 of 100, compared to 1 of 100.) It is not possible to compare the RLA model output with Cooper's forecasts because Cooper works only with the catchment area of this particular center.

Plishkin develops a series of linear difference equations, combined with a Markov framework, to forecast the need for dialysis beds in Massachusetts. He assumes a treatment incidence of 40 million in 1972 and 45 million in 1973. A number of other assumptions about rates of transplant, mortality and the like are made, largely on the advice of experts and from medical publications. It is difficult to evaluate his assumptions about the benchmark data used, since his source, the Inter-Hospital Dialysis Group apparently was unwilling to release figures to the public (p.326) Nevertheless, it is possible to compare the assumed growth rates in Plishkins' figures with those generated by the RLA model. To accomplish this comparison, it was found necessary to combine patient numbers in states 3 through 5 to match against Plishkins' "on dialysis" state. Further, Plishkins' states "first year living donor transplant, first year cadaver donor transplant and carrying transplant for more than on year" were combined to give the number of successful transplants carried in the system. RLA states 2 (stable) and 6 (transplant) were combined to produce a comparable figure. Since Plishkin's forecasts indicate numbers in a year, RLA observations were totaled for December, 1972 and December, 1973.

The absolute values in Table 6-2 show Plishkin's estimates exceed the RLA estimates, but RLA rates of change between the two years, particularly for dialysis, exceed the rate of change that Plishkin forecasts. The RLA short fall in absolute values

cannot be explained simply in terms of the RTI undercount problem, since the dialysis and transplant estimates have been inflated by a factor that eliminates the discrepancy between RTI and California Kidney Disease Information System figures. The RLA estimates, based upon these calculations, still fall short of Plishkin's "informed experts' " estimates, with the exception of the 1973 Bayesian estimate of dialysis patients. Until more accurate incidence data can be found, it will be impossible to assess the relative validities of the two figures. The maximum likelihood based forecasts show smaller rates of increase than do the Bayesian forecasts. Thus Bayesian forecasts deviate further from Plishkin's forecasts of expansion than do the MLE forecasts.

Transplanted patients constitute 45 % of the total chronic patients, according to the RLA forecast, in 1972, and 33% in 1973. Plishkin's estimates show 43% transplanted cases in 1972, growing to 47% in 1973. The Bayesian estimates shrink RLA's percentages to 34% and 28% respectively. One can only speculate on the reasons for this discrepancy. The drop from 1972 to 1973 in part results from the fact that though RTI transplant coverage remains fairly constant, dialysis coverage drops dramatically. Thus, inflated dialysis estimates grow more from 1972 to 1973 than do inflated transplant estimates.

Since it is impossible to verify the accuracy of Plishkin's benchmark data figures, and since Plishkin makes no attempt to check the accuracy of his forecasts against data for Massachusetts, it is impossible to compare the RLA and Plishkin model as forecasting tools. RLA is confident that the principle of statistical estimation is preferable as data collection is improved.

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Table -2

Comparison of Plishkin and RLA Forecast of Dialysis
and Transplant Patients: Plishkin (Massachusetts)
RLA (Boston Megalopolis)

		1972	1973	%Δ
Dialysis				
On Dialysis (States) 3, 4, 5)	P	600.0[1]	706.0[1]	+17.7%
RLA -		290.0[2a]	653.0[2a]	+31.1%
		481.0[2b]	1143.0[2b]	+38.6%

	1972	1973		1972	1973	%Δ
Transplants						
First year living donor transplant	112.0	126.0	P	452.0[1]	632.0[1]	+39.8
			MLE	238.0[2a]	324.0[2a]	+36.4
			Bayes	246.0[2b]	441.0[2b]	+54.9
First year cadaver donor transplant	160.0	180.0				
Carrying transplant for more than one year	180.0	326.0				

Sources: (1) Plishkin REF (339)

(2) RTI data
Computed by Roy Littlejohn Associates, Inc.

a. Maximum likelihood technique.

b. Bayesian technique.

Note: These estimates have been adjusted upward by the extent of the RTI undercount, as given in Table 2-2.

Nakamura and Parker modeled the kidney disease - treatment system as part of a larger control model based on linear programming principles. They hoped to provide a framework within which policy makers could decide on optimum treatment strategies, given cost minimizing and/or life maximizing goals. As a further refinement, they discussed the implications of control over the size of the transition probabilities themselves, presumably through expenditure on medical research and technological development.[1]

As a description of the treatment systems structure, the Nakamura-Parker model provides an extensive and logical state space. Currently, however, the model has been operated to simulate system behavior, using coefficients constructed from published figures and expert consultation. The structural parameters are thus plausible, in a general sense, but not testable estimates drawn from empirical data.[2]

The Committee on Chronic Kidney Disease, in its final report issued in 1967 (the Gottschalk Report) REF (260) made a forecast of dialysis - transplant needs for the nation as a whole. Though it is impossible to use the Gottschalk Report's results to project regional figures, some general comparisons with the RLA forecasts can be made.

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[1]RLA compared the states of the Nakamura-Parker Markov matrix with the RLA model in Interim Report No. 2.

[2]The most interesting possibility discussed by Nakamura and Parker, policy control over the state transition probabilities, was not tested by simulation in their paper.

In a general way, the Committee's study tried to account for system interaction much as a Markov or stochastic approach would do. However, the output of the Committee's efforts lacks institutional detail. They forecasted dialysis and transplantation needs over the period 1968-1977, without specifying dialysis treatment mix. Coefficients used for forecasting were, once again, based on available expert opinion. Though their incidence measures were bracketed by confidence intervals, this technique here seems to be imposed artifically on figures computed from data of unknown distribution.

The model Gottschalk used is essentially a series of projections of dialysis case loads and transplantation requirements based on high, expected and low incidence estimates, and high, expected (probable) and zero rates of transplantation. (Assumptions behind the values used are detailed in Chapter on "Incidence", and in Appendix C of the Gottschalk Report.) Table 6-3 shows the Gottschalk projections, under the various assumptions. Note that, as proved true with the Plishkin comparison, the RLA model forecasts increases both in dialysis and in transplant treatments that exceed the Gottschalk projections under any assumption.

Summary

Most attempts to use Markov techniques in the study of disease treatment systems have tested their results with data drawn from clinical experience, with limited general applicability, or have estimated model coefficients from expert opinion. Both

Table 6-3

Projected Dialysis and Transplant Patients, Level and Change, 1972 - 73

	Dialysis Patient Years			Transplants		
Patients:	1972	1973	%Δ	1972	1973	%Δ
Probable number of transplants						
Lower number of cases	27,293	24,325	14.2%	1,200	1,440	20.0%
Most probable number of cases	25,096	28,728	14.5%	1,300	1,440	20.0%
Upper number of cases	29,727	34,088	14.7%	1,200	1,440	20.0%
Maximum number of transplants						
Lower number of cases	20,584	23,141	12.4%	2,000	2,400	20.0%
Most probable number of cases	29,017	32,905	13.4%	2,000	2,400	20.0%
Upper number of cases	24,387	27,544	12.9%	2,000	2,930	20.0%
No Transplants						
Lower number of cases	23,191	26,847	15.8%			
Most probable number of cases	26,954	31,252	15.8%			
Upper number of cases	31,624	36,611	15.8%			

*Transplants during year and patients.

Source: Report of the Committee on Chronic Kidney Disease (1967)

Plishkin, and Nakamura and Parker prefer to simulate conditions under certain plausible assumptions rather than estimate parameters statistically. Cooper, on the other hand, estimates parameters statistically but his model is geographically limited in scope.

The Gottschalk report, which involves sophisticated extra polation based on a variety of assumptions, provides useful fore-casted data, as does Plishkin. In comparison with these studies the RLA model estimates parameters from large volumes of collected regionally based data. The model gives higher estimates of the rate of increase in dialysis and transplant patients. This occurs, despite an apparent tendency, especially in states 5 and 6, to undercount the absolute numbers in states of the system.

CHAPTER SEVEN

VII. SUMMARY AND CONCLUSION

Governmental responsibility for the treatment of chronic kidney patients has expanded in recent years, and with it the need for effective health planning tools. Recent federal legislation permits reimbursement for eighty per cent of treatment charges for end-stage renal patients. The National Health Planning and Development and Health Facilities Assistance Act charges health planning agencies with area-based planning responsibilities. These and similar measures at the state level occasion the need for an understanding of the dynamics of the health care delivery system for kidney patients.

The model presented in this report is one methodological approach to the formulation of a regionally-based, statistically-derived model of the flows of patients in and out of the various kidney treatment modalities. The formulation is couched in terms of time-based transitions of patients as input to and outputs from the various treatment/health states. Parameters are derived from existing data to estimate the monthly probabilities of a patient entering a new state out of an existing state or condition. Using the assumptions of the Markov model that equilibrium distributions of patients throughout the system are independent of time, the model user can forecast future flows of patients, given initial population distributions by region, age and sex.

The RLA model incorporates the dynamic processes of

birth, migration and aging into the total forecast model. Seven treatment states are used: well, stable after transplant, home dialysis, peritoneal dialysis, institutional dialysis, transplant and death. Parameter estimates of transition probabilities are made separately for three region types: a megalopolis (Boston-Worcester-Providence), a group of rural states (Mississippi, Tennessee, Virginia, North and South Carolina), and a large state (California.) It is hoped that health planners can use the statistical estimates from that region most similar to their own.

The specific values of the transition matrixes are discussed in Chapter 3. Of particular interest is the evidence to support the view that a steady state exists. (See Chapter 4.) Wide variations by region are evident. Fifty-three per cent of Southern patients remain on home dialysis in the long run, compared to sixteen per cent in California and only eight per cent in Boston. More patients in Boston (56%) and California (50%) remain stable following transplant than is true for the South (32%.) Longrun forecasts show that 35% will be on institutional dialysis in Boston, 33% in California but only 13% in the South.

The input-output model is useful as a planning tool to take account not only of the direct impacts of a given policy but also the indirect impacts as patients in one treatment require others as well. For example, taking the direct and indirect effects together, Southern patients' lifetime costs for kidney care are projected to average $50,000, compared to $79,000 for Boston and $87,000 for California. The Southern

figure is less than other regions not alone because of its greater relative reliance on home dialysis, but also because of its relatively shorter life expectancy. See Chapter 5 for a discussion of these points.

Data for parameter estimation were collected from the Research Triangle Institute's National Dialysis Registry, from the American College of Surgeons'Organ Transplant Registry, and from state sources. Data used for parameter estimation came from the RTI source, since despite problems of coverage the form of collection and recording of these data best fit the requirements of the RLA model.

Parameters were estimated in two ways: the classical maximum likelihood technique, and the Bayesian technique. Results were presented for each of four age groups, by region. A breakdown by sex was computed, but not used extensively in analysis, because repeated subclassification of the data reduced many parameter estimate to meaninglessness. Parameters were estimated first from a 25% sample. The results were combined with the well state, and inflated by a factor of four.

With reservations, the authors have offered incidence estimates andspecific forecasts based upon available data from the National Dialysis Registry. Because of apparent underreporting to the Registry, the RLA model does not very accurately predict total patient flows as estimated from independent sources. More research needs to be done to collect data for correct incidence estimates. This data problem should, however, have no necessarily

adverse effect on the estimation of transition probabilities, unless the non-responses are systematic within age/region/sex breakdowns. More refinements of the model would be possible if greater detail on dialysis treatments were available from good data sources on transplants (American College of Surgeons) or if better transplant data were available in the files of the National Dialysis Registry.

The RLA model was compared with other systems, and found to be somewhat unique. Models built to describe kidney treatment using Markovian assumptions differ from RLA in one of the two respects: use of parameters estimated non-statistically from "expert opinion" (Plishkin, Nakamura/Parker) or estimation of parameters for a single treatment center only (Farrow, Cooper.) A comparison of RLA and Cooper's empirical results shows wide areas of agreement on parameter values. See Chapter 6.

The staff used California data and data provided by the Social Security Administration to estimate costs of kidney treatment. This exercise yielded two products discussed in Chapter 5:

1) A test of the hypothesis that average cost of treatment does not vary with scale of operations. The test showed that scale economies do exist for institutional hemodialysis, using California data on a small number of centers.

2) Average treatment costs, by region and age, for home and instituional hemodialysis, using data from the Social Security Administration.

Data on transplant costs were inadequate for estimation. An

average figure was taken from a recent General Accounting Office study.

Cost averages were combined with steady state distributions and state occupancy statistics to compute expected monthly patient costs and expected lifetime patient costs by region. A companion report presents econometric analysis of dialysis cost results.

Though standardizing data collection and extending coverage of data files would improve the chances of accurate forecasting with the model, RLA feels that the current model should serve as a useful input/output description of kidney related health services. As such it may be a useful planning tool at least in the short run for regional health planners interested in understanding the interactive flows of patients through the renal health care treatment system.

APPENDIX A

Technical Discussion of Forecast Model Structure

TableA-1 presents a step-by-step development of the forecasting matrix, $P^{(t)}$, which begins with the basic 7 X 7 disease treatment matrix $P^{(c)}$, and builds in birth, migration and aging assumptions.

Using the $P^{(f)}$ forecasting matrix, it is possible to examine the steady state properties of this input-output system. Following Ortiz and Parker, let us define:

$$g(t) = \sum_a \sum_i N_i^a(t) / N_i^a(t-1) - 1, \quad a = 1 \ldots 4, \; i = 1 \ldots 7$$

where N_i^a represents total system members in disease category i, age group a.

$$g(t)_{\lim t \to \infty} = g$$

Since $\lambda_1 = \sum_a \sum_i N_i^a(t) / N_i^a(t-1)$, $\lim t \to \infty$

clearly $\lambda_1 - 1 = g$

Steady state growth will be conditioned only by the steady state system inputs (birth, in-migration) and outputs (death and out-migration), so that

$g = \beta - \delta$

β = steady state input rate

δ = steady state output rate

We now need expressions for β and δ to solve for g(and λ)

Let b^a_{ii} and $m'^a_{ii} = 0$, for all a and i, and recall that $\sum_i z^a_i$ distributes survivors across age classes. The expression for now becomes

$$\lambda = \sum_a \sum_i \sum_j p^a_{ij} \; z^a_i$$

If $P^{(c)a} = \left| p^a \right|$ is primitive, as defined, then limiting

absolute probabilities exist, $p_i(t \rightarrow \infty)$ 0, and are components of the normalized right eigenvector of $P^{(C)}$ associated with an

Thus $\lim_{t \to \infty} p^a_{ij}(t) = p^a_i$ $a = 1 \ldots 4$, $i;j = 1 \ldots . 7$

in steady state matrix form

$$\begin{vmatrix} p_1 & \cdots & \cdots & p_1 \\ p_1 & \cdots & \cdots & p_1 \\ \vdots & & & \\ p_1 & \cdots & \cdots & p_1 \end{vmatrix}$$

which may be diagonalized

$$IP^{(c)} \text{ (steady state)} = 1Z_i$$

where $Z_i = \lim_{t \to \infty} N^a_i(t) / \sum_i N^a_i(t)$

This result allocates survivors in each age group across disease states. An approximate solution for the system's expansion by age <u>and</u> disease would be $\lambda_1 (Z^a)$ (Zi). This expression treats steady state age and disease distributions as independent phenomena. A more precise formulation would specify the interaction between the aging process and disease distribution, a dynamic relationship which adds mathematical complexity to the problem.

Let $\beta = \sum_{a}\sum_{i}(b^{a}_{ii} + m'^{a}_{ii})\, Z^{a}_{i}$

and $\delta = \sum_{a}\sum_{i}(1 - \sum_{j} p^{a}_{ij})\, Z^{a}_{i}$

$a = 1...4$
$i,j = 1.......7$

where $\sum_{i} Z^{a}_{i} = \lim_{t} \sum_{i} N^{a}_{i}(t) / \sum_{a}\sum_{i} N^{a}_{i}(t) = Z^{a}$

and $1 - \sum_{j} p^{a}_{ij}$ is the age-specific death rate.

Since $g = \beta - \delta$

Then $g = \sum_{a}\sum_{i}(b^{a}_{ii} + m'^{a}_{ii} + \sum_{j} p^{a}_{ij})\, Z^{a}_{i} - 1$

and $\lambda_1 = \sum_{a}\sum_{i}(b^{a}_{ii} + m'^{a}_{ii} + \sum_{j} p^{a}_{ij})\, Z^{a}_{i}$

Here, if $P^{(b)}$ is a primitive matrix (no absorbing or periodic elements, all elements positive), then

$$ZP^{(b)} = \lambda_1 Z$$

λ_1 is the largest eigenvalue of $P^{(b)}$ and Z is a right eigenvector, with elements Z^{a}.

λ_1 converts the elements of Z into steady state, age-specific growth rates. It will be useful to examine the steady state properties of the distribution of individuals across disease-treatment states as well.

TABLE *I* -1

Structure of Forecasting Model

Structure (1)

	Description	State Numbers	Conditions
1.	$P^{(c)}$ - fundamental disease treatment matrix, P_{ij} elements $i = 1, \ldots 7$ $j = 1, \ldots 7$	7 x 7 State 7 absorbing	$P_{71}, P_{72}, \ldots P_{76} = 0$ $P_{77} = 1.0$ $\sum_{j=1}^{7} P_{ij} = 1.0$
	$P^{(d)}$ - non-normalized survivor matrix, P_{ij} elements $i = 1, \ldots 6$ $j = 1, \ldots 6$	6 x 6 No absorbing state	$\sum_{j=1}^{6} P_{ij} \leq 1.0$
2.	$P^{(d)}\ a,a$ = stayer matrix $a = 1 \ldots 4$ each element $= (1 - \alpha) P^{a}_{ij}$ $i = 1 \ldots 6$, $j = 1 \ldots 6$	6 x 6	$\sum_{j=1}^{6} P_{ij} \leq 1.0$ $\alpha \leq 1.0$
	$P^{(d)}\ a,a+1$ = mover matrix $a = 1 \ldots 4$ each element $= \alpha P^{a}_{ij}$ $i = 1 \ldots 6$, $j = 1 \ldots 6$	6 x 6	Same $P^{(d)}\ 4,5$ is that portion of Q appropriate to age group 4.
	$P^{(b)}$ = matrix for aging the population (no input - each element = $P^{(d)a,a}$ or $P^{(d)}\ a,a+1$	24 x 24	Same

Table A-1 Continued
Structure (1)

Structure

$$\left|\begin{array}{ccc|c} P_{11}, & P_{12} \cdots\cdots\cdots & P_{16} & P_{17} \\ \vdots & & & \\ P_{61}, & P_{62} \cdots\cdots\cdots & P_{66} & P_{67} \\ \hline P_{71}, & P_{72} \cdots\cdots\cdots & P_{76} & P_{77} \end{array}\right| = \left|P\right|^{(c)} = \left|\begin{array}{c|c} \left|P\right|^{(d)} & Q \\ \hline 0 & I \end{array}\right|$$

$$\left|\begin{array}{ccccc} P^{(d)11} & P^{(d)12} & 0 & 0 & 0 \\ 0 & P^{(d)22} & P^{(d)23} & \vdots & \vdots \\ \vdots & 0 & P^{(d)33} & P^{(d)34} & \vdots \\ \vdots & \vdots & 0 & P^{(d)44} & \vdots \\ \vdots & \vdots & \vdots & \vdots & \vdots \\ 0 & 0 & 0 & 0 & 0 \end{array}\right| = P^{(b)}$$

Table A-1 Continued

Structure (2)

3. $P^{(a)}$ = Disease treatment matrix which ages the population (no population input)

28 X 28

4 age-specific absorbing states (state 7)

$$\sum_{j=1}^{7} P_{ij} = 1.0$$

Qa - 28 age - specific death rates

$$\begin{array}{r} i = 28 \\ i = 4 \end{array}\left[\begin{array}{c|c} P^{(b)} & Qa \\ \hline 0 & I \end{array}\right] = P^{(}$$

3. $P^{(f)}$ The forecast model

Input coefficients:

1. Birth

b^{a}_{i1} - Column vector adding proportion of existing population to age 1, state 1

2. In-migration

m^{aa}_{ii} - Adds to diagonal term of stayer matrix

$$\left[\begin{array}{c|c} \begin{matrix} b^{1}_{11} \\ \vdots \\ b^{1}_{61} \\ b^{2}_{11} \\ \vdots \\ b^{2}_{61} \\ b^{3}_{11} \\ \vdots \\ b^{3}_{61} \\ b^{4}_{11} \\ \vdots \\ b^{4}_{61} \end{matrix} & 0 \\ \hline 0 & 0 \end{array}\right] + \left[\begin{array}{c|c} \begin{matrix} m^{11}_{11} & & & & & & & \\ & \ddots & & & & & & \\ & & m^{11}_{66} & & & & & \\ & & & m^{22}_{11} & & & & \\ & & & & \ddots & & & \\ & & & & & m^{22}_{66} & & \\ & & & & & & m^{33}_{11} & \\ & & & & & & & \ddots \\ & & & & & & & & m^{33}_{66} \\ & & & & & & & & & m^{44}_{11} \\ & & & & & & & & & & \ddots \\ & & & & & & & & & & & m^{44}_{66} \end{matrix} & 0 \\ \hline 0 & 0 \end{array}\right] + \left[\begin{array}{c|c} P^{(b)} & Qa \\ \hline 0 & I \end{array}\right]$$

APPENDIX B

Maximum Likelihood Estimation of Model Parameters

The process may be described as equivalent to observing n individuals in state i, i= 1 to 7 at time (t-1), with multinomial transition probabilities $P_{ij}(t)$ that are either stationary or variable over time. A trial yields the numbers n_{ij} at (t) which are sufficient statistics for the estimates P_{ij} (The approach set forth below is due primarily to Anderson and Goodman).

Formally,

$$m(\,p_{ij}(t);\; n_{ij}(t),\; n_i(t-1)) = n_i(t-1)\,!/\prod_j n_{ij}(t)\,!\;\prod_j p_{ij}(t)^{n_{ij}(t)}$$

i, j= 1.....s

t = 1.....T

the conditional distribution of $n_{ij}(t)$ given $n_i(t-1)$

For long sequences, when members of the system of seven states can be held constant (no input or output adjustment to the n's), and given a fair presumption of homogeneity, it is reasonable to estimate.

$$p_{ij} = \sum_{1}^{T} n_{ij}(t) / \sum_{0}^{T-1} n_i(t)$$

In our case, however, it will be preferable not to prejudge the p's, but rather to estimate, often from diverse and short sequences, probabilities dependent on time,

$$p_{ij}(t) = n_{ij}(t) / \sum_{k=1}^{S} n_{ik}(t)$$

testing for the truth of the null hypothesis:

$$H_o : \hat{p}_{ij}(t) = \hat{p}_{ij}$$

Appendix C

Bayesian Estimation of Model Parameters
by Benjamin Moultrie

Bayes' theorem provides a very powerful tool for statistical inference. Bayesian estimation procedures allow one to make use of prior knowledge, in the appropriate probabilistic terms, about the model which is operating. Conversely, the classical method of inference (i.e., max. likelihood, etc.) requires perfect information about the model and at the same time no information about the the values of the parameters of the model. For example, it would be paradoxical to say that the kidney disease model is Markovian and at the same time to say we have no information about the movement of patients through the "modeled system".

The Bayesian method in statistics is usually presented as follows: Consider the joint probability density function $f(X,\Theta)$ defined on the product space $X \cdot \Theta$, where $X = \{X\}$ denotes the sample space, and $\Theta = \{\Theta\}$ denotes the parameter space.

If one decomposes the joint density $f(X,\Theta))$ in a conditional density $f(X|\Theta)$ and a marginal density $f(\Theta)$ it follows from Bayes' theorem that

$$f(\Theta|X) = \frac{f(\Theta)\,f(X|\Theta)}{\int f(\Theta)\,f(X|\Theta)\,d\Theta}$$

Notice that Bayes' theorem uses two inputs under the form of density functions. The first input is the marginal density function $f(\Theta)$ defined "prior" to the observation. The second input is the density function of the observation conditional to a given value of This function $f(X|\Theta)$ viewed as a function of Θ, for a given sample, is the likelihood function of classical statistics. The output of

Bayes' theorem is the posterior density function $f(\Theta|X)$ (e.g., $f(\Theta|X)$ is sometimes denoted $L(\Theta|X)$). Probability judgements on Θ, and of future values of X will be made according to this posterior density function.

The first step consists in choosing a density that represents satisfactorily our prior knowledge. "Non-informative" priors are usually defined by invariance principle. The "non-informative"priors of the type mentioned above take the form of an uniform density on the range of Θ.

While the "non-informative" priors are said to maximize the degree of entropy (or uncertainty) with respect to Θ, "informative" priors can be defined by families of natural conjugate prior densities for the most common data generating processes (i.e., Binomial, Poisson, Normal, etc.). However, a serious problem is confronted when a prior distribution is constructed. Not only are meaningful distributions highly complex, they are also somewhat arbitrary and clearly subjective. Since the data presented in most cases are exceedingly weak and ambiguous without a subjective basis for analysis, no analysis could occur at all.

The arbitrariness in prior construction remains a very troubling feature of Bayesian analysis. Nevertheless, the problem of identifying the relevant model for kidney disease cannot be achieved in a straightforward classical sense. In other words, the limitations of sampling techniques dictate the use of the "postdictive" inference induced by the Bayesian framework. For example, if a reasonable size sample

yields a zero state probability, is it true that the state is empty? Clearly, prior information or intuition would negate the possibility that the sample represents the true state of the world.

The data-generating process signifies, "prior to experimentation," that the model under study is a N state model with N-1 transient states and one trapping state. Thus, if the first N-1 states is a set of transient states for a "closed system" $P_{ij} \longrightarrow 0$ as $n \longrightarrow \infty$ for all i,i and there exists no stationary distribution, where n represents the number of time epochs and i and j the states occupied at n-1 and n respectively. In terms of deterministic theory, if the system is "open," the general properties of equilibrium distributions across states implies that in stochastic means the model estimated will have some renewal characteristics. Therefore, one basic assumption is that the rate of injection into the system represents a steady state process.

It is necessary to determine whether or not the transition probabilities of the system are independent of time.
The technique suggests a quadratic loss function ($L = (\Theta - \hat{\Theta})^2$) and a Matrix Beta probabilistic model where

$$E(P_{ij}|n) \quad \frac{n_{ij} + a_{ij}}{\sum_{j=1}^{r} (n_{ij} + a_{ij})} = \frac{n_{ij} + a_{ij}}{c_i}$$

and

$$\mathrm{Var}(P_{ij}|n) = \frac{E(P_{ij}|n)(1 - E(P_{ij}|n)}{c_i + 1}$$

where n_{ij} = the observed numbers passing from state i to state j

a_{ij} = the expected numbers, based on prior distribution.

The prior distribution used in the RLA estimates is presented in Table C-1.

Table C-1
Bayesian Estimates:
Prior State Distribution, Absorption
Probabilities and Transition Matrix

Initial State Distribution

State	1	2	3	4	5	6
%	.1666000	.1666000	.1666000	.1666000	.1666000	.1666000

Absorption Probabilities

P_{17}	P_{27}	P_{37}	P_{47}	P_{57}	P_{67}	P_{77}
.1424200	.1424200	.1424200	.1424200	.1424200	.1424200	1.0000000

Prior Transition Matrix

	1	2	3	4	5	6	7
1	.1715160		.1715160	.1715160	.1715160	.1715160	.1424200
2		.1715160	.1715160	.1715160	.1715160	.1715160	.1424200
3			.2143950	.2143950	.2143950	.2143950	.1424200
4			.2143950	.2143950	.2143950	.2143950	.1424200
5			.2143950	.2143950	.2143950	.2143950	.1424200
6		.1715160	.1715160	.1715160	.1715160	.1715160	.1424200
7							1.0000000

Appendix D

Parameter Estimation From General Population Statistics

Data from general population records were used two ways:

1) To estimate certain parameters applicable to the "well" population (state 1);

2) To estimate birth, migration and aging coefficient for the forecasting process.

Linking the well population with other parameter estimates required an estimate of transition probabilities P_{11} and P_{17}, as well as some assumption about "incidence" of treated end stage kidney failure. To develop a population base, RLA used Census projections for states, divided into the four age categories, for January, 1972 (by interpolation between July 1971 and July 1972). Region 1 totals were divided by assuming that SMSA percentages of Massachusetts and Rhode Island populations remained constant from 1970 to 1972, and adjusting state totals accordingly. Regions 2 and 3 projections were developed totally from state data. Sex breakdowns were computed by applying 1970 $\frac{\text{Male}}{\text{Total Population}}$, $\frac{\text{Female}}{\text{Total Population}}$, ratios by age and state, to the January 1972 totals. Population totals appear in Table 1-1.

Death out of the well population was calculated by summing the deaths, by age groups, state and sex, from <u>Vital Statistics</u> (1970) and subtracting deaths due to chronic kidney disease. A conservative procedure was used here: only deaths due to "chronic and unqualified nephritis and renal sclerosis" (582-584) were

counted in the adjustment. One might argue persuasively for inclusion of "hypertensive heart and renal disease" (404), "infections of the kidney" and others. These total deaths, adjusted for chronic kidney deaths, were transformed into deaths/100,000 and applied to the January, 1972 population figures to produce an estimate of the number of deaths, by sex, age, and region, from the well population in 1972. (Note: infant deaths were subtracted from the estimate of age group 1 on grounds that the prime interest was in the experience of cohort members alive at the beginning of 1972). Yearly death totals were then adjusted to monthly totals.

Totals moving from state 1 to states of the chronic disease system were estimated using values computed from RTI data. Since RLA worked from a 25% sample, monthly transitions were multiplied by 4.

The results of the above work produced monthly transitions in row 1 of the basic Markov matrix. Totals here were combined with transitions data for the rest of the system to estimate time-dependent and homogeneous monthly transitions matrixes.

Birth coefficients were estimated from the 1972 projected crude birth rate/1000 total population of 15.6. Infant mortality, assumed 22.1/1000 live births, was used to adjust the birth rate for first-year survival. The yearly live birth total was converted to a monthly value and divided equally among the model's 24 age-specific states.

Lacking adequate data on in- and out-migration that were specific to the disease-treatment categories used, RLA computed net

migration rates and added them to diagonal elements of the "Stayer" matrixes. The Region 1 estimate of zero net migration was based on the Census analysis of in- and out-migration in New England from 1965 to 1970. Regions 2 and 3 were more difficult to pinpoint. Net migration for the "South Atlantic" states and the "East South Central" states were combined to provide an estimate for Region 2. Region 3 net migration is the value applicable to the "Pacific" region.

Appendix E: Chi-Square Test of Homogeneity

It is possible to test the assumption that parameters in this system are homogeneous, or independent of the order in a sequence in which transitions occur, by using a simultaneous confidence test.

If one adjusts the number of degrees of freedom used for the number of parameters assumed structurally greater than zero, then the test is similar to a conventional chi-square test on a contingency table with elements

$$P_{11}^{(1)},\ P_{12}^{(1)},\ P_{13}^{(1)}\ \ldots\ldots\ldots P_{ij}^{(1)}$$

$$P_{11}^{(2)},\ P_{12}^{(2)},\ P_{13}^{(2)}\ \ldots\ldots\ldots P_{ij}^{(2)}$$

to be contrasted to the row

$$P_{11},\ P_{12},\ P_{13}\ \ldots\ldots\ldots\ldots\ldots\ldots P_{ij}$$

If $\hat{P}_{ij}$ is the observedvaluecalculated for each time period and P_{ij} is the expected stationary value (for which substitute $\hat{P}_{ij}$) then one may accept or reject the null hypothesis that the homogeneous and non-homogeneous probabilities differ at a 95% confidence level using the formula

$$\sum_{t}\ \sum_{j}\ N_i(t-1)\ (\hat{P}_{ij}(t) - \hat{P}_{ij})^2/P_{ij} \leq \chi_i^{2\ .05}$$

with (S-1)(T-1) degrees of freedom

$i = 1, 2 \ldots\ldots S$
$t = 1, 2 \ldots\ldots T$

APPENDIX F

Steady State Probabilities and State Occupancy Statistics

A steady state solution for a system of a stochastic nature depends on characteristics of the matrix described in Appendix A. Here, the computational technique used is discussed, and the steady state solutions are related to mean recurrence times.

If P_j is the steady state probability for $j = 1 \ldots 6$, then the result $P_j = \sum_{i=1}^{6} P_i P_{ij}$ obtains. This means that there are 6 equations, with each P_i entered and weighted by the appropriate one-step probability P_{ij}. For computation purposes, these six equations are linear combinations of each other, and thus have no unique solution. A solution is possible, however, if a new equation replace one of the six. The appropriate equation uses the basic probability rule:

$$\sum_{i=1}^{6} P_i = 1$$

With the reconstituted six equations, the P_j's may be computed.

The reader will notice that 6 states appear in this discussion of the steady state. The seventh absorbing state, death, was removed because no solution is possible with it, short of the

trivial case of $P_1, \ldots P_6 = 0$, $P_7 = 1.0$. One must interpret the 6 - state limiting probabilities as the long run distribution of the "survivors" in a disease-treatment system. As such, of course, it is at best a "medium-run" set of probabilities. Survivor probabilities are, of course, normalized to sum to one.

Patients move about in the system in a manner governed by the underlying probability processes. The average time it takes a patient to return to a state, once the state is left, is called the mean recurrence time. Obviously, states in which patients spend the most time should show a low mean recurrence time. In fact, the mean recurrence time relates to the limiting-state (steady state) probabilities:

$$\bar{\Theta}_{jj} = \frac{1}{P_j} \quad j = 1 \ldots 6 \text{ where } \bar{\Theta}_j, = \text{mean recurrence times.}$$

Other state occupancy statistics of interest describe the expected time in a state (mean holding time) and the expected time in a state before moving to some other state (mean first passage time).

It can be shown that the holding time in state 1 has a geometric distribution. That being the case, the mean holding time $\bar{h}_i$, is simply the mean of the geometric distribution:

$$\bar{h}_i = (1 - p_{ii})^{-1}$$

The expected total time spent in the transient portion of the system (time until absorption) is then

$$h = \sum_i (1 - p_{ii})^{-1}$$

Mean first passage times are related to each other by the equation:

$$\bar{f}_{ij} = 1 + \sum_{\substack{k=1 \\ k \neq j}}^{6} p_{ik} \bar{f}_{kj}$$

Thus it is possible to compute first passage times from a system of simultaneous equations, utilizing the one-step transition probabilities. The transitions can occur from states 2 - 6 into states 2 - 7. Thus a representative equation for this system would be

$$\bar{f}_{23} = 1 + p_{22} \bar{f}_{23} + p_{24} \bar{f}_{43} + p_{25} \bar{f}_{53} + p_{26} \bar{f}_{63}$$

$$(\bar{f}_{73} \equiv 0, \text{ by definition})$$

Notice the relation of this expression to the mean holding time -

$$\bar{f}_{23} = \frac{1}{1 - p_{22}} + p_{24} \bar{f}_{43} + p_{25} \bar{f}_{53} + p_{26} \bar{f}_{63}$$

The state holding time is thus a weighted average of first passage times from the state.

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